INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :
C12N 15/12, C07K 14/47, 16/18, 19/00, C12N 15/62, A61K 38/17, 39/395, 48/00, C12N 5/08, G01N 33/574, C12Q 1/68

A2

(11) International Publication Number: WO 00/61753

(43) International Publication Date: 19 October 2000 (19.10.00)

(21) International Application Number: PCT/US00/09312

(22) International Filing Date: 7 April 2000 (07.04.00)

(30) Priority Data:

09/289,198	9 April 1999 (09.04.99)	US
09/429,755	28 October 1999 (28.10.99)	US
09/534,825	23 March 2000 (23.03.00)	US

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(81) Designated States: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

Without international search report and to be republished upon receipt of that report.

(54) Title: COMPOSITIONS AND METHODS FOR THE TREATMENT AND DIAGNOSIS OF BREAST CANCER

(57) Abstract

Compositions and methods for the detection and therapy of breast cancer are disclosed. The compounds provided include nucleotide sequences that are preferentially expressed in breast tumor tissue, as well as polypeptides encoded by such nucleotide sequences. Vaccines and pharmaceutical compositions comprising such compounds are also provided and may be used, for example, for the prevention and treatment of breast cancer. The polypeptides may also be used for the production of antibodies, which are useful for diagnosing and monitoring the progression of breast cancer in a patient.

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COMPOSITIONS AND METHODS FOR THE TREATMENT AND DIAGNOSIS OF BREAST CANCER

TECHNICAL FIELD

The present invention relates generally to the detection and therapy of breast cancer. The invention is more specifically related to nucleotide sequences that are preferentially expressed in breast tumor tissue and to polypeptides encoded by such nucleotide sequences. The nucleotide sequences and polypeptides may be used in vaccines and pharmaceutical compositions for the prevention and treatment of breast cancer. The polypeptides may also be used for the production of compounds, such as antibodies, useful for diagnosing and monitoring the progression of breast cancer in a patient.

BACKGROUND OF THE INVENTION

Breast cancer is a significant health problem for women in the United States and throughout the world. Although advances have been made in detection and treatment of the disease, breast cancer remains the second leading cause of cancer-related deaths in women, affecting more than 180,000 women in the United States each year. For women in North America, the life-time odds of getting breast cancer are now one in eight.

No vaccine or other universally successful method for the prevention or treatment of breast cancer is currently available. Management of the disease currently relies on a combination of early diagnosis (through routine breast screening procedures) and aggressive treatment, which may include one or more of a variety of treatments such as surgery, radiotherapy, chemotherapy and hormone therapy. The course of treatment for a particular breast cancer is often selected based on a variety of prognostic parameters, including an analysis of specific tumor markers. *See, e.g.*, Porter-Jordan and Lippman, *Breast Cancer 8*:73-100 (1994). However, the use of established markers often leads to a result that is difficult to interpret, and the high mortality observed in

breast cancer patients indicates that improvements are needed in the treatment, diagnosis and prevention of the disease.

Accordingly, there is a need in the art for improved methods for therapy and diagnosis of breast cancer. The present invention fulfills these needs and further provides other related advantages.

SUMMARY OF THE INVENTION

Briefly stated, the subject invention provides compositions and methods for the diagnosis and therapy of breast cancer. In one aspect, isolated polynucleotides are provided, comprising (a) a nucleotide sequence preferentially expressed in breast cancer tissue, relative to normal tissue; (b) a variant of such a sequence, as defined below; or (c) a nucleotide sequence encoding an epitope of a polypeptide encoded by at least one of the above sequences. In one embodiment, the isolated polynucleotide comprises a human endogenous retroviral sequence recited in SEQ ID NO:1. In other embodiments, the isolated polynucleotide comprises a sequence recited in any one of SEQ ID NO: 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317.

In related embodiments, the isolated polynucleotide encodes an epitope of a polypeptide, wherein the polypeptide is encoded by a nucleotide sequence that: (a) hybridizes to a sequence recited in any one of SEQ ID NO: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 under stringent conditions; and (b) is at least 80% identical to a sequence recited in any one of SEQ ID NO: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317.

In another embodiment, the present invention provides an isolated polynucleotide encoding an epitope of a polypeptide, the polypeptide being encoded by: (a) a nucleotide sequence transcribed from the sequence of SEQ ID NO: 141; or (b) a variant of said nucleotide sequence that contains one or more nucleotide substitutions, deletions, insertions and/or modifications at no more than 20% of the nucleotide positions, such that the antigenic and/or immunogenic properties of the polypeptide encoded by the nucleotide sequence are retained. Isolated DNA and RNA molecules comprising a nucleotide sequence complementary to a polynucleotide as described above are also provided.

In related aspects, the present invention provides recombinant expression vectors comprising a polynucleotide as described above and host cells transformed or transfected with such expression vectors.

In further aspects, polypeptides comprising an amino acid sequence encoded by a polynucleotide as described above, and monoclonal antibodies that bind to such polypeptides are provided. In certain embodiments, the inventive polypeptides comprise an amino acid sequence selected from the group consisting of SEQ ID NO: 299, 300, 304-306, 308 and 315, and variants thereof as defined below.

In yet another aspect, methods are provided for determining the presence of breast cancer in a patient. In one embodiment, the method comprises detecting, within a biological sample, a polypeptide as described above. In another embodiment, the method comprises detecting, within a biological sample, an RNA molecule encoding a polypeptide as described above. In yet another embodiment, the method comprises (a) intradermally injecting a patient with a polypeptide as described above; and (b) detecting an immune response on the patient's skin and therefrom detecting the presence of breast cancer in the patient. In further embodiments, the present invention provides methods for determining the presence of breast cancer in a patient as described above wherein the polypeptide is encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242, 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289, 290 and sequences that hybridize thereto under stringent conditions.

In a related aspect, diagnostic kits useful in the determination of breast cancer are provided. The diagnostic kits generally comprise either one or more monoclonal antibodies as described above, or one or more monoclonal antibodies that bind to a polypeptide encoded by a nucleotide sequence selected from the group consisting of sequences provided in SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242 and 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289, 290 and a detection reagent.

Diagnostic kits are also provided that comprise a first polymerase chain reaction primer and a second polymerase chain reaction primer, at least one of the primers being specific for a polynucleotide described herein. In one embodiment, at least one of the primers comprises at least about 10 contiguous nucleotides of a polynucleotide as described above, or a polynucleotide encoding a polypeptide encoded by a sequence selected from the group consisting of SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289 and 290.

Within another related aspect, the diagnostic kit comprises at least one oligonucleotide probe, the probe being specific for a polynucleotide described herein. In one embodiment, the probe comprises at least about 15 contiguous nucleotides of a polynucleotide as described above, or a polynucleotide selected from the group consisting of SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289 and 290.

In another related aspect, the present invention provides methods for monitoring the progression of breast cancer in a patient. In one embodiment, the method comprises: (a) detecting an amount, in a biological sample, of a polypeptide as described above at a first point in time; (b) repeating step (a) at a subsequent point in time; and (c) comparing the amounts of polypeptide detected in steps (a) and (b), and therefrom monitoring the progression of breast cancer in the patient. In another embodiment, the method comprises (a) detecting an amount, within a biological sample, of an RNA molecule encoding a polypeptide as described above at a first point in time; (b) repeating

step (a) at a subsequent point in time; and (c) comparing the amounts of RNA molecules detected in steps (a) and (b), and therefrom monitoring the progression of breast cancer in the patient. In yet other embodiments, the present invention provides methods for monitoring the progression of breast cancer in a patient as described above wherein the polypeptide is encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242, 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289, 290 and sequences that hybridize thereto under stringent conditions.

In still other aspects, pharmaceutical compositions, which comprise a polypeptide as described above in combination with a physiologically acceptable carrier, and vaccines, which comprise a polypeptide as described above in combination with an immunostimulant or adjuvant, are provided. In yet other aspects, the present invention provides pharmaceutical compositions and vaccines comprising a polypeptide encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 78-86, 144, 145, 153, 167, 177, 193, 199, 205, 208, 215, 217, 220, 241, 242 and 246, 248, 249, 252, 256, 267, 270, 274, 277, 279, 282, 283, 285-287, 289, 290 and sequences that hybridize thereto under stringent conditions.

In related aspects, the present invention provides methods for inhibiting the development of breast cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as described above.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows the differential display PCR products, separated by gel electrophoresis, obtained from cDNA prepared from normal breast tissue (lanes 1 and 2) and from cDNA prepared from breast tumor tissue from the same patient (lanes 3 and 4). The arrow indicates the band corresponding to B18Ag1.

Figure 2 is a northern blot comparing the level of B18Ag1 mRNA in breast tumor tissue (lane 1) with the level in normal breast tissue.

Figure 3 shows the level of B18Ag1 mRNA in breast tumor tissue compared to that in various normal and non-breast tumor tissues as determined by RNase protection assays.

Figure 4 is a genomic clone map showing the location of additional retroviral sequences obtained from ends of XbaI restriction digests (provided in SEQ ID NO:3 - SEQ ID NO:10) relative to B18Ag1.

Figures 5A and 5B show the sequencing strategy, genomic organization and predicted open reading frame for the retroviral element containing B18Ag1.

Figure 6 shows the nucleotide sequence of the representative breast tumor-specific cDNA B18Ag1.

Figure 7 shows the nucleotide sequence of the representative breast tumor-specific cDNA B17Ag1.

Figure 8 shows the nucleotide sequence of the representative breast tumor-specific cDNA B17Ag2.

Figure 9 shows the nucleotide sequence of the representative breast tumor-specific cDNA B13Ag2a.

Figure 10 shows the nucleotide sequence of the representative breast tumor-specific cDNA B13Ag1b.

Figure 11 shows the nucleotide sequence of the representative breast tumor-specific cDNA B13Ag1a.

Figure 12 shows the nucleotide sequence of the representative breast tumor-specific cDNA B11Ag1.

Figure 13 shows the nucleotide sequence of the representative breast tumor-specific cDNA B3CA3c.

Figure 14 shows the nucleotide sequence of the representative breast tumor-specific cDNA B9CG1.

Figure 15 shows the nucleotide sequence of the representative breast tumor-specific cDNA B9CG3.

Figure 16 shows the nucleotide sequence of the representative breast tumor-specific cDNA B2CA2.

Figure 17 shows the nucleotide sequence of the representative breast tumor-specific cDNA B3CA1.

Figure 18 shows the nucleotide sequence of the representative breast tumor-specific cDNA B3CA2.

Figure 19 shows the nucleotide sequence of the representative breast tumor-specific cDNA B3CA3.

Figure 20 shows the nucleotide sequence of the representative breast tumor-specific cDNA B4CA1.

Figure 21A depicts RT-PCR analysis of breast tumor genes in breast tumor tissues (lanes 1-8) and normal breast tissues (lanes 9-13) and H_2O (lane 14).

Figure 21B depicts RT-PCR analysis of breast tumor genes in prostate tumors (lane 1, 2), colon tumors (lane 3), lung tumor (lane 4), normal prostate (lane 5), normal colon (lane 6), normal kidney (lane 7), normal liver (lane 8), normal lung (lane 9), normal ovary (lanes 10, 18), normal pancreases (lanes 11, 12), normal skeletal muscle (lane 13), normal skin (lane 14), normal stomach (lane 15), normal testes (lane 16), normal small intestine (lane 17), HBL-100 (lane 19), MCF-12A (lane 20), breast tumors (lanes 21-23), H_2O (lane 24), and colon tumor (lane 25).

Figure 22 shows the recognition of a B11Ag1 peptide (referred to as B11-8) by an anti-B11-8 CTL line.

Figure 23 shows the recognition of a cell line transduced with the antigen B11Ag1 by the B11-8 specific clone A1.

Figure 24 shows recognition of a lung adenocarcinoma line (LT-140-22) and a breast adenocarcinoma line (CAMA-1) by the B11-8 specific clone A1.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the diagnosis, monitoring and therapy of breast cancer. The compositions described herein include polypeptides, polynucleotides and antibodies.

Polypeptides of the present invention generally comprise at least a portion of a protein that is expressed at a greater level in human breast tumor tissue than in normal breast tissue (*i.e.*, the level of RNA encoding the polypeptide is at least 2-fold higher in tumor tissue). Such polypeptides are referred to herein as breast tumor-specific polypeptides, and cDNA molecules encoding such polypeptides are referred to as breast tumor-specific cDNAs. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of a polypeptide as described above, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or fragments thereof, that are capable of binding to a portion of a polypeptide as described above. Antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies.

Polypeptides within the scope of this invention include, but are not limited to, polypeptides (and epitopes thereof) encoded by a human endogenous retroviral sequence, such as the sequence designated B18Ag1 (Figure 5 and SEQ ID NO:1). Also within the scope of the present invention are polypeptides encoded by other sequences within the retroviral genome containing B18Ag1 (SEQ ID NO: 141). Such sequences include, but are not limited to, the sequences recited in SEQ ID NO:3 - SEQ ID NO:10. B18Ag1 has homology to the *gag* p30 gene of the endogenous human retroviral element S71, as described in Werner et al., *Virology 174*:225-238 (1990) and also shows homology to about thirty other retroviral gag genes. As discussed in more detail below, the present invention also includes a number of additional breast tumor-specific polypeptides, such as those encoded by the nucleotide sequences recited in SEQ ID NO: 11-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317.

As used herein, the term "polypeptide" encompasses amino acid chains of any length, including full length proteins containing the sequences recited herein. A

polypeptide comprising an epitope of a protein containing a sequence as described herein may consist entirely of the epitope, or may contain additional sequences. The additional sequences may be derived from the native protein or may be heterologous, and such sequences may (but need not) possess immunogenic or antigenic properties.

An "epitope," as used herein is a portion of a polypeptide that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Epitopes may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides derived from the native polypeptide for the ability to react with antigen-specific antisera and/or T-cell lines or clones. An epitope of a polypeptide is a portion that reacts with such antisera and/or T-cells at a level that is similar to the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. B-cell and T-cell epitopes may also be predicted via computer analysis. Polypeptides comprising an epitope of a polypeptide that is preferentially expressed in a tumor tissue (with or without additional amino acid sequence) are within the scope of the present invention.

The term "polynucleotide(s)," as used herein, means a single or double-stranded polymer of deoxyribonucleotide or ribonucleotide bases and includes DNA and corresponding RNA molecules, including HnRNA and mRNA molecules, both sense and anti-sense strands, and comprehends cDNA, genomic DNA and recombinant DNA, as well as wholly or partially synthesized polynucleotides. An HnRNA molecule contains introns and corresponds to a DNA molecule in a generally one-to-one manner. An mRNA molecule corresponds to an HnRNA and DNA molecule from which the introns have been excised. A polynucleotide may consist of an entire gene, or any portion thereof. Operable anti-sense polynucleotides may comprise a fragment of the corresponding polynucleotide, and the definition of "polynucleotide" therefore includes all such operable anti-sense fragments.

The compositions and methods of the present invention also encompass variants of the above polypeptides and polynucleotides.

A polypeptide "variant," as used herein, is a polypeptide that differs from the recited polypeptide only in conservative substitutions and/or modifications, such that the antigenic properties of the polypeptide are retained. In a preferred embodiment, variant polypeptides differ from an identified sequence by substitution, deletion or addition of five amino acids or fewer. Such variants may generally be identified by modifying one of the above polypeptide sequences, and evaluating the antigenic properties of the modified polypeptide using, for example, the representative procedures described herein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described below) to the identified polypeptides.

As used herein, a "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. In general, the following groups of amino acids represent conservative changes: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his.

Variants may also, or alternatively, contain other modifications, including the deletion or addition of amino acids that have minimal influence on the antigenic properties, secondary structure and hydropathic nature of the polypeptide. For example, a polypeptide may be conjugated to a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (*e.g.*, poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

A nucleotide "variant" is a sequence that differs from the recited nucleotide sequence in having one or more nucleotide deletions, substitutions or

additions. Such modifications may be readily introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis as taught, for example, by Adelman et al. (*DNA*, 2:183, 1983). Nucleotide variants may be naturally occurring allelic variants, or non-naturally occurring variants. Variant nucleotide sequences preferably exhibit at least about 70%, more preferably at least about 80% and most preferably at least about 90% identity (determined as described below) to the recited sequence.

The breast tumor antigens provided by the present invention include variants that are encoded by DNA sequences which are substantially homologous to one or more of the DNA sequences specifically recited herein. "Substantial homology," as used herein, refers to DNA sequences that are capable of hybridizing under moderately stringent conditions. Suitable moderately stringent conditions include prewashing in a solution of 5X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5X SSC, overnight or, in the event of cross-species homology, at 45°C with 0.5X SSC; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. Such hybridizing DNA sequences are also within the scope of this invention, as are nucleotide sequences that, due to code degeneracy, encode an immunogenic polypeptide that is encoded by a hybridizing DNA sequence.

Two nucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acid residues in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment

schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Resarch Foundaiton, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenes pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) Fast and sensitive multiple sequence alignments on a microcomputer *CABIOS 5*:151-153; Myers, E.W. and Muller W. (1988) Optimal alignments in linear space *CABIOS 4*:11-17; Robinson, E.D. (1971) *Comb. Theor 11*:105; Santou, N. Nes, M. (1987) The neighbor joining method. A new method for reconstructing phylogenetic trees *Mol. Biol. Evol. 4*:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) Rapid similarity searches of nucleic acid and protein data banks *Proc. Natl. Acad., Sci. USA 80*:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (i.e. gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e. the window size) and multiplying the results by 100 to yield the percentage of sequence identity. In general, polynucleotides encoding all or a portion of the polypeptides described herein may be prepared using any of several techniques. For example, cDNA molecules encoding such polypeptides may be cloned on the basis of the breast tumor-specific expression of the corresponding mRNAs, using differential display PCR. This technique compares the amplified products from RNA template prepared from normal and breast tumor tissue. cDNA may

be prepared by reverse transcription of RNA using a $(dT)_{12}AG$ primer. Following amplification of the cDNA using a random primer, a band corresponding to an amplified product specific to the tumor RNA may be cut out from a silver stained gel and subcloned into a suitable vector (*e.g.*, the T-vector, Novagen, Madison, WI). Polynucleotides encoding all or a portion of the breast tumor-specific polypeptides disclosed herein may be amplified from cDNA prepared as described above using the random primers shown in SEQ ID NO.:87-125.

Alternatively, a polynucleotide encoding a polypeptide as described herein (or a portion thereof) may be amplified from human genomic DNA, or from breast tumor cDNA, via polymerase chain reaction. For this approach, B18Ag1 sequence-specific primers may be designed based on the sequence provided in SEQ ID NO:1, and may be purchased or synthesized. One suitable primer pair for amplification from breast tumor cDNA is (5'ATG GCT ATT TTC GGG GGC TGA CA) (SEQ ID NO:126) and (5'CCG GTA TCT CCT CGT GGG TAT T) (SEQ ID NO:127). An amplified portion of B18Ag1 may then be used to isolate the full length gene from a human genomic DNA library or from a breast tumor cDNA library, using well known techniques, such as those described in Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY (1989). Other sequences within the retroviral genome of which B18Ag1 is a part may be similarly prepared by screening human genomic libraries using B18Ag1-specific sequences as probes. Nucleotides translated into protein from the retroviral genome shown in SEQ ID NO: 141 may then be determined by cloning the corresponding cDNAs, predicting the open reading frames and cloning the appropriate cDNAs into a vector containing a viral promoter, such as T7. The resulting constructs can be employed in a translation reaction, using techniques known to those of skill in the art, to identify nucleotide sequences which result in expressed protein. Similarly, primers specific for the remaining breast tumor-specific polypeptides described herein may be designed based on the nucleotide sequences provided in SEQ ID NO:11-86, 142-298, 301-303, 307, 313, 314, 316 and 317.

Recombinant polypeptides encoded by the DNA sequences described above may be readily prepared from the DNA sequences. For example, supernatants

from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

In general, any of a variety of expression vectors known to those of ordinary skill in the art may be employed to express recombinant polypeptides of this invention. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a polynucleotide that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO.

Such techniques may also be used to prepare polypeptides comprising epitopes or variants of the native polypeptides. For example, variants of a native polypeptide may generally be prepared using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis, and sections of the DNA sequence may be removed to permit preparation of truncated polypeptides. Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. *See* Merrifield, *J. Am. Chem. Soc.* 85:2149-2146 (1963). Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division, Foster City, CA, and may be operated according to the manufacturer's instructions.

In specific embodiments, polypeptides of the present invention encompass amino acid sequences encoded by a polynucleotide having a sequence recited in any one of SEQ ID NO:1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255,

257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317, and variants of such polypeptides. Polypeptides within the scope of the present invention also include polypeptides (and epitopes thereof) encoded by DNA sequences that hybridize to a sequence recited in any one of SEQ ID NO:1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 under stringent conditions, wherein the DNA sequences are at least 80% identical in overall sequence to a recited sequence and wherein RNA corresponding to the nucleotide sequence is expressed at a greater level in human breast tumor tissue than in normal breast tissue. As used herein, "stringent conditions" refers to prewashing in a solution of 6X SSC, 0.2% SDS; hybridizing at 65°C, 6X SSC, 0.2% SDS overnight; followed by two washes of 30 minutes each in 1X SSC, 0.1% SDS at 65°C and two washes of 30 minutes each in 0.2 X SSC, 0.1% SDS at 65°C. Polynucleotides according to the present invention include molecules that encode any of the above polypeptides.

In another aspect of the present invention, antibodies are provided. Such antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In one such technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.*, mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for the antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519 (1976), and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Antibodies may be used, for example, in methods for detecting breast cancer in a patient. Such methods involve using an antibody to detect the presence or absence of a breast tumor-specific polypeptide as described herein in a suitable biological sample. As used herein, suitable biological samples include tumor or normal tissue biopsy, mastectomy, blood, lymph node, serum or urine samples, or other tissue, homogenate, or extract thereof obtained from a patient.

There are a variety of assay formats known to those of ordinary skill in the art for using an antibody to detect polypeptide markers in a sample. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, the assay may be performed in a Western blot format, wherein a protein preparation from the biological sample is submitted to gel electrophoresis, transferred to a suitable membrane and allowed to react with the antibody. The presence of the antibody on the membrane may then be detected using a suitable detection reagent, as described below.

In another embodiment, the assay involves the use of antibody immobilized on a solid support to bind to the polypeptide and remove it from the remainder of the sample. The bound polypeptide may then be detected using a second antibody or reagent that contains a reporter group. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized antibody after incubation of the antibody with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the antibody is indicative of the reactivity of the sample with the immobilized antibody, and as a result, indicative of the concentration of polypeptide in the sample.

The solid support may be any material known to those of ordinary skill in the art to which the antibody may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose filter or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681.

The antibody may be immobilized on the solid support using a variety of techniques known to those in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the antigen and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a

well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the antibody, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of antibody ranging from about 10 ng to about 1 μg, and preferably about 100-200 ng, is sufficient to immobilize an adequate amount of polypeptide.

Covalent attachment of antibody to a solid support may also generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the antibody. For example, the antibody may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.*, Pierce Immunotechnology Catalog and Handbook (1991) at A12-A13).

In certain embodiments, the assay for detection of polypeptide in a sample is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the biological sample, such that the polypeptide within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a second antibody (containing a reporter group) capable of binding to a different site on the polypeptide is added. The amount of second antibody that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation

time) is that period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with breast cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include enzymes (such as horseradish peroxidase), substrates, cofactors, inhibitors, dyes, radionuclides, luminescent groups, fluorescent groups and biotin. The conjugation of antibody to reporter group may be achieved using standard methods known to those of ordinary skill in the art.

The second antibody is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound second antibody is then removed and bound second antibody is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of breast cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value established from non-tumor tissue. In one preferred embodiment, the cut-off value is the average mean signal

obtained when the immobilized antibody is incubated with samples from patients without breast cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value may be considered positive for breast cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, p. 106-7 (Little Brown and Co., 1985). Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for breast cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the antibody is immobilized on a membrane, such as nitrocellulose. In the flow-through test, the polypeptide within the sample bind to the immobilized antibody as the sample passes through the membrane. A second, labeled antibody then binds to the antibody-polypeptide complex as a solution containing the second antibody flows through the membrane. The detection of bound second antibody may then be performed as described above. In the strip test format, one end of the membrane to which antibody is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second antibody and to the area of immobilized antibody. Concentration of second antibody at the area of immobilized antibody indicates the presence of breast cancer. Typically, the concentration of second antibody at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of antibody immobilized on the membrane is selected to generate a visually

discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μg, and more preferably from about 50 ng to about 1 μg. Such tests can typically be performed with a very small amount of biological sample.

The presence or absence of breast cancer in a patient may also be determined by evaluating the level of mRNA encoding a breast tumor-specific polypeptide as described herein within the biological sample (*e.g.*, a biopsy, mastectomy and/or blood sample from a patient) relative to a predetermined cut-off value. Such an evaluation may be achieved using any of a variety of methods known to those of ordinary skill in the art such as, for example, *in situ* hybridization and amplification by polymerase chain reaction.

For example, polymerase chain reaction may be used to amplify sequences from cDNA prepared from RNA that is isolated from one of the above biological samples. Sequence-specific primers for use in such amplification may be designed based on the sequences provided in any one of SEQ ID NO: 1, 11-86, 142-298 301-303, 307, 313, 314, 316 and 317, and may be purchased or synthesized. In the case of B18Ag1, as noted herein, one suitable primer pair is B18Ag1-2 (5'ATG GCT ATT TTC GGG GGC TGA CA) (SEQ ID NO:126) and B18Ag1-3 (5'CCG GTA TCT CCT CGT GGG TAT T) (SEQ ID NO:127). The PCR reaction products may then be separated by gel electrophoresis and visualized according to methods well known to those of ordinary skill in the art. Amplification is typically performed on samples obtained from matched pairs of tissue (tumor and non-tumor tissue from the same individual) or from unmatched pairs of tissue (tumor and non-tumor tissue from different individuals). The amplification reaction is preferably performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the tumor sample as compared to the same dilution of the non-tumor sample is considered positive.

As used herein, the term "primer/probe specific for a polynucleotide" means an oligonucleotide sequence that has at least about 80% identity, preferably at least about 90% and more preferably at least about 95%, identity to the polynucleotide in question, or an oligonucleotide sequence that is anti-sense to a sequence that has at least about 80% identity, preferably at least about 90% and more preferably at least about 95%, identity to the polynucleotide in question. Primers and/or probes which may be usefully employed in the inventive diagnostic methods preferably have at least about 10-40 nucleotides. In a preferred embodiment, the polymerase chain reaction primers comprise at least about 10 contiguous nucleotides of a polynucleotide that encodes one of the polypeptides disclosed herein or that is anti-sense to a sequence that encodes one of the polypeptides disclosed herein. Preferably, oligonucleotide probes for use in the inventive diagnostic methods comprise at least about 15 contiguous oligonucleotides of a polynucleotide that encodes one of the polypeptides disclosed herein or that is anti-sense to a sequence that encodes one of the polypeptides disclosed herein. Techniques for both PCR based assays and *in situ* hybridization assays are well known in the art.

Conventional RT-PCR protocols using agarose and ethidium bromide staining, while important in defining gene specificity, do not lend themselves to diagnostic kit development because of the time and effort required in making them quantitative (i.e., construction of saturation and/or titration curves), and their sample throughput. This problem is overcome by the development of procedures such as real time RT-PCR which allows for assays to be performed in single tubes, and in turn can be modified for use in 96 well plate formats. Instrumentation to perform such methodologies are available from Perkin Elmer/Applied Biosystems Division. Alternatively, other high throughput assays using labeled probes (e.g., digoxygenin) in combination with labeled (e.g., enzyme fluorescent, radioactive) antibodies to such probes can also be used in the development of 96 well plate assays.

In yet another method for determining the presence or absence of breast cancer in a patient, one or more of the breast tumor-specific polypeptides described may be used in a skin test. As used herein, a "skin test" is any assay performed directly on a patient in which a delayed-type hypersensitivity (DTH) reaction (such as swelling,

reddening or dermatitis) is measured following intradermal injection of one or more polypeptides as described above. Such injection may be achieved using any suitable device sufficient to contact the polypeptide or polypeptides with dermal cells of the patient, such as a tuberculin syringe or 1 mL syringe. Preferably, the reaction is measured at least 48 hours after injection, more preferably 48-72 hours.

The DTH reaction is a cell-mediated immune response, which is greater in patients that have been exposed previously to a test antigen (*i.e.*, an immunogenic portion of a polypeptide employed, or a variant thereof). The response may measured visually, using a ruler. In general, a response that is greater than about 0.5 cm in diameter, preferably greater than about 5.0 cm in diameter, is a positive response, indicative of breast cancer.

The breast tumor-specific polypeptides described herein are preferably formulated, for use in a skin test, as pharmaceutical compositions containing at least one polypeptide and a physiologically acceptable carrier, such as water, saline, alcohol, or a buffer. Such compositions typically contain one or more of the above polypeptides in an amount ranging from about 1 μg to 100 μg, preferably from about 10 μg to 50 μg in a volume of 0.1 mL. Preferably, the carrier employed in such pharmaceutical compositions is a saline solution with appropriate preservatives, such as phenol and/or Tween 80™.

In other aspects of the present invention, the progression and/or response to treatment of a breast cancer may be monitored by performing any of the above assays over a period of time, and evaluating the change in the level of the response (*i.e.*, the amount of polypeptide or mRNA detected or, in the case of a skin test, the extent of the immune response detected). For example, the assays may be performed every month to every other month for a period of 1 to 2 years. In general, breast cancer is progressing in those patients in whom the level of the response increases over time. In contrast, breast cancer is not progressing when the signal detected either remains constant or decreases with time.

In further aspects of the present invention, the compounds described herein may be used for the immunotherapy of breast cancer. In these aspects, the

compounds (which may be polypeptides, antibodies or polynucleotides) are preferably incorporated into pharmaceutical compositions or vaccines. Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds in combination with an immunostimulant, such as an adjuvant or a liposome (into which the compound is incorporated). An immunostimulant may be any substance that enhances or potentiates an immune response (antibody and/or cell-mediated) to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

Alternatively, a vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. In such vaccines, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*, vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science 259*:1745-1749 (1993), and reviewed by

Cohen, *Science 259*:1691-1692 (1993). The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (*e.g.*, polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bortadella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (*e.g.*, IFN-γ, TNFα, IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (*e.g.*, IL-4, IL-5, IL-6 and IL-10) tend to favor the

induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Corixa Corporation (Seattle, WA; *see* US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555 and WO 99/33488. Immunostimulatory DNA sequences are also described, for example, by Sato et al., *Science* 273:352, 1996. Another preferred adjuvant is a saponin, preferably QS21 (Aquila Biopharmaceuticals Inc., Framingham, MA), which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprise an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Other preferred adjuvants include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (*e.g.*, SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Ribi ImmunoChem Research Inc., Hamilton, MT), RC-529 (Ribi ImmunoChem Research Inc., Hamilton, MT) and Aminoalkyl glucosaminide 4-phosphates (AGPs).

Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immunostimulant and a suitable carrier or excipient. The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides, for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology (*see, e.g.*, Coombes et al., *Vaccine 14*:1429-1438, 1996) and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane.

Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. Such carriers include microparticles of poly(lactide-co-glycolide), as well as polyacrylate, latex, starch, cellulose and dextran. Other delayed-release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (*e.g.*, a cross-linked polysaccharide or oligosaccharide) and, optionally, an external layer comprising an amphiphilic compound, such as a phospholipid (*see e.g.*, U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA

haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature 392*:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med. 50*:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med. 4*:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNFα to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNFα, CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible

intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fcγ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a polypeptide of the present invention (or portion or other variant thereof) such that the polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

Vaccines and pharmaceutical compositions may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are preferably hermetically sealed to preserve sterility of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a vaccine or pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier

immediately prior to use.

The above pharmaceutical compositions and vaccines may be used, for example, for the therapy of breast cancer in a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with breast cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of breast cancer or to treat a patient afflicted with breast cancer. In a preferred embodiment, the compounds are administered either prior to or following surgical removal of primary tumors and/or treatment by administration of radiotherapy and conventional chemotherapeutic drugs. To prevent or slow the development of breast cancer, a pharmaceutical composition or vaccine comprising one or more polypeptides as described herein may be administered to a patient. Alternatively, naked DNA or plasmid or viral vector encoding the polypeptide may be administered. For treating a patient with breast cancer, the pharmaceutical composition or vaccine may comprise one or more polypeptides, antibodies or polynucleotides complementary to DNA encoding a polypeptide as described herein (*e.g.*, antisense RNA or antisense deoxyribonucleotide oligonucleotides).

Routes and frequency of administration, as well as dosage, will vary from individual to individual. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Between 1 and 10 doses may be administered for a 52-week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical

compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 100 µg to 5 mg. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

Polypeptides disclosed herein may also be employed in adoptive immunotherapy for the treatment of cancer. Adoptive immunotherapy may be broadly classified into either active or passive immunotherapy. In active immunotherapy, treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (for example, tumor vaccines, bacterial adjuvants, and/or cytokines).

In passive immunotherapy, treatment involves the delivery of biologic reagents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T lymphocytes (for example, CD8+ cytotoxic T-lymphocyte, CD4+ T-helper, tumor-infiltrating lymphocytes), killer cells (Natural Killer cells, lymphokine-activated killer cells), B cells, or antigen presenting cells (such as dendritic cells and macrophages) expressing the disclosed antigens. The polypeptides disclosed herein may also be used to generate antibodies or anti-idiotypic antibodies (as in U.S. Patent No. 4,918,164), for passive immunotherapy.

The predominant method of procuring adequate numbers of T-cells for adoptive immunotherapy is to grow immune T-cells *in vitro*. Culture conditions for expanding single antigen-specific T-cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. These *in vitro* culture conditions typically utilize intermittent stimulation with antigen, often in the presence of cytokines, such as IL-2, and non-dividing feeder cells. As noted above, the immunoreactive polypeptides described herein may be used to rapidly expand antigen-specific T cell cultures in order to generate sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage or B-cells, may be pulsed with immunoreactive polypeptides or transfected with a polynucleotide sequence(s), using

standard techniques well known in the art. For cultured T-cells to be effective in therapy, the cultured T-cells must be able to grow and distribute widely and to survive long term *in vivo*. Studies have demonstrated that cultured T-cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al. *Ibid*).

The polypeptides disclosed herein may also be employed to generate and/or isolate tumor-reactive T-cells, which can then be administered to the patient. In one technique, antigen-specific T-cell lines may be generated by *in vivo* immunization with short peptides corresponding to immunogenic portions of the disclosed polypeptides. The resulting antigen specific CD8+ CTL clones may be isolated from the patient, expanded using standard tissue culture techniques, and returned to the patient.

Alternatively, peptides corresponding to immunogenic portions of the polypeptides may be employed to generate tumor reactive T cell subsets by selective *in vitro* stimulation and expansion of autologous T cells to provide antigen-specific T cells which may be subsequently transferred to the patient as described, for example, by Chang et al. *(Crit. Rev. Oncol. Hematol., 22*(3), 213, 1996).

In another embodiment, syngeneic or autologous dendritic cells may be pulsed with peptides corresponding to at least an immunogenic portion of a polypeptide disclosed herein. The resulting antigen-specific dendritic cells may either be transferred into a patient, or employed to stimulate T cells to provide antigen-specific T cells which may, in turn, be administered to a patient. The use of peptide-pulsed dendritic cells to generate antigen-specific T cells and the subsequent use of such antigen-specific T cells to eradicate tumors in a murine model has been demonstrated by Cheever et al. ("Therapy With Cultured T Cells: Principles Revisited," *Immunological Reviews, 157*:177, 1997).

Additionally vectors expressing the disclosed polynucleotides may be introduced into stem cells taken from the patient and clonally propagated *in vitro* for autologous transplant back into the same patient. In one embodiment, cells of the immune system, such as T cells, may be isolated from the peripheral blood of a patient, using a commercially available cell separation system, such as CellPro Incorporated's (Bothell,

WA) CEPRATE™ system (see U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). The separated cells are stimulated with one or more of the immunoreactive polypeptides contained within a delivery vehicle, such as a microsphere, to provide antigen-specific T cells. The population of tumor antigen-specific T cells is then expanded using standard techniques and the cells are administered back to the patient.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLES

EXAMPLE 1

PREPARATION OF BREAST TUMOR-SPECIFIC CDNAS USING DIFFERENTIAL DISPLAY RT-PCR

This Example illustrates the preparation of cDNA molecules encoding breast tumor-specific polypeptides using a differential display screen.

A. Preparation of B18Ag1 cDNA and Characterization of mRNA Expression

Tissue samples were prepared from breast tumor and normal tissue of a patient with breast cancer that was confirmed by pathology after removal from the patient. Normal RNA and tumor RNA was extracted from the samples and mRNA was isolated and converted into cDNA using a $(dT)_{12}AG$ (SEQ ID NO:130) anchored 3' primer. Differential display PCR was then executed using a randomly chosen primer (CTTCAACCTC) (SEQ ID NO:103). Amplification conditions were standard buffer containing 1.5 mM $MgCl_2$, 20 pmol of primer, 500 pmol dNTP, and 1 unit of *Taq* DNA polymerase (Perkin-Elmer, Branchburg, NJ). Forty cycles of amplification were performed using 94°C denaturation for 30 seconds, 42°C annealing for 1 minute, and 72° C extension for 30 seconds. An RNA fingerprint containing 76 amplified products was

obtained. Although the RNA fingerprint of breast tumor tissue was over 98% identical to that of the normal breast tissue, a band was repeatedly observed to be specific to the RNA fingerprint pattern of the tumor. This band was cut out of a silver stained gel, subcloned into the T-vector (Novagen, Madison, WI) and sequenced.

The sequence of the cDNA, referred to as B18Ag1, is provided in SEQ ID NO:1. A database search of GENBANK and EMBL revealed that the B18Ag1 fragment initially cloned is 77% identical to the endogenous human retroviral element S71, which is a truncated retroviral element homologous to the Simian Sarcoma Virus (SSV). S71 contains an incomplete *gag* gene, a portion of the *pol* gene and an LTR-like structure at the 3' terminus (*see* Werner et al., *Virology 174*:225-238 (1990)). B18Ag1 is also 64% identical to SSV in the region corresponding to the P30 (gag) locus. B18Ag1 contains three separate and incomplete reading frames covering a region which shares considerable homology to a wide variety of gag proteins of retroviruses which infect mammals. In addition, the homology to S71 is not just within the *gag* gene, but spans several kb of sequence including an LTR.

B18Ag1-specific PCR primers were synthesized using computer analysis guidelines. RT-PCR amplification (94°C, 30 seconds; 60°C → 42°C, 30 seconds; 72°C, 30 seconds for 40 cycles) confirmed that B18Ag1 represents an actual mRNA sequence present at relatively high levels in the patient's breast tumor tissue. The primers used in amplification were B18Ag1-1 (CTG CCT GAG CCA CAA ATG) (SEQ ID NO:128) and B18Ag1-4 (CCG GAG GAG GAA GCT AGA GGA ATA) (SEQ ID NO:129) at a 3.5 mM magnesium concentration and a pH of 8.5, and B18Ag1-2 (ATG GCT ATT TTC GGG GCC TGA CA) (SEQ ID NO:126) and B18Ag1-3 (CCG GTA TCT CCT CGT GGG TAT T) (SEQ ID NO:127) at 2 mM magnesium at pH 9.5. The same experiments showed exceedingly low to nonexistent levels of expression in this patient's normal breast tissue (*see* Figure 1). RT-PCR experiments were then used to show that B18Ag1 mRNA is present in nine other breast tumor samples (from Brazilian and American patients) but absent in, or at exceedingly low levels in, the normal breast tissue corresponding to each cancer patient. RT-PCR analysis has also shown that the B18Ag1 transcript is not present in various normal tissues (including lymph node, myocardium

and liver) and present at relatively low levels in PBMC and lung tissue. The presence of B18Ag1 mRNA in breast tumor samples, and its absence from normal breast tissue, has been confirmed by Northern blot analysis, as shown in Figure 2.

The differential expression of B18Ag1 in breast tumor tissue was also confirmed by RNase protection assays. Figure 3 shows the level of B18Ag1 mRNA in various tissue types as determined in four different RNase protection assays. Lanes 1-12 represent various normal breast tissue samples, lanes 13-25 represent various breast tumor samples; lanes 26-27 represent normal prostate samples; lanes 28-29 represent prostate tumor samples; lanes 30-32 represent colon tumor samples; lane 33 represents normal aorta; lane 34 represents normal small intestine; lane 35 represents normal skin, lane 36 represents normal lymph node; lane 37 represents normal ovary; lane 38 represents normal liver; lane 39 represents normal skeletal muscle; lane 40 represents a first normal stomach sample, lane 41 represents a second normal stomach sample; lane 42 represents a normal lung; lane 43 represents normal kidney; and lane 44 represents normal pancreas. Interexperimental comparison was facilitated by including a positive control RNA of known β-actin message abundance in each assay and normalizing the results of the different assays with respect to this positive control.

RT-PCR and Southern Blot analysis has shown the B18Ag1 locus to be present in human genomic DNA as a single copy endogenous retroviral element. A genomic clone of approximately 12-18 kb was isolated using the initial B18Ag1 sequence as a probe. Four additional subclones were also isolated by XbaI digestion. Additional retroviral sequences obtained from the ends of the XbaI digests of these clones (located as shown in Figure 4) are shown as SEQ ID NO:3 - SEQ ID NO:10, where SEQ ID NO:3 shows the location of the sequence labeled 10 in Figure 4, SEQ ID NO:4 shows the location of the sequence labeled 11-29, SEQ ID NO:5 shows the location of the sequence labeled 3, SEQ ID NO:6 shows the location of the sequence labeled 6, SEQ ID NO:7 shows the location of the sequence labeled 12, SEQ ID NO:8 shows the location of the sequence labeled 13, SEQ ID NO:9 shows the location of the sequence labeled 14 and SEQ ID NO:10 shows the location of the sequence labeled 11-22.

Subsequent studies demonstrated that the 12-18 kb genomic clone contains a retroviral element of about 7.75 kb, as shown in Figures 5A and 5B. The sequence of this retroviral element is shown in SEQ ID NO: 141. The numbered line at the top of Figure 5A represents the sense strand sequence of the retroviral genomic clone. The box below this line shows the position of selected restriction sites. The arrows depict the different overlapping clones used to sequence the retroviral element. The direction of the arrow shows whether the single-pass subclone sequence corresponded to the sense or anti-sense strand. Figure 5B is a schematic diagram of the retroviral element containing B15Ag1 depicting the organization of viral genes within the element. The open boxes correspond to predicted reading frames, starting with a methionine, found throughout the element. Each of the six likely reading frames is shown, as indicated to the left of the boxes, with frames 1-3 corresponding to those found on the sense strand.

Using the cDNA of SEQ ID NO:1 as a probe, a longer cDNA was obtained (SEQ ID NO:227) which contains minor nucleotide differences (less than 1%) compared to the genomic sequence shown in SEQ ID NO:141.

B. Preparation of cDNA Molecules Encoding Other Breast Tumor-Specific Polypeptides

Normal RNA and tumor RNA was prepared and mRNA was isolated and converted into cDNA using a $(dT)_{12}AG$ anchored 3' primer, as described above. Differential display PCR was then executed using the randomly chosen primers of SEQ ID NO: 87-125. Amplification conditions were as noted above, and bands observed to be specific to the RNA fingerprint pattern of the tumor were cut out of a silver stained gel, subcloned into either the T-vector (Novagen, Madison, WI) or the pCRII vector (Invitrogen, San Diego, CA) and sequenced. The sequences are provided in SEQ ID NO:11 - SEQ ID NO:86. Of the 79 sequences isolated, 67 were found to be novel (SEQ ID NO:11-26 and 28-77) (*see also* Figures 6-20).

An extended DNA sequence (SEQ ID NO: 290) for the antigen B15Ag1 (originally identified partial sequence provided in SEQ ID NO: 27) was obtained in further studies. Comparison of the sequence of SEQ ID NO: 290 with those in the gene bank as described above, revealed homology to the known human β-A activin gene.

Further studies led to the isolation of the full-length cDNA sequence for the antigen B21GT2 (also referred to as B311D; originally identified partial cDNA sequence provided in SEQ ID NO: 56). The full-length sequence is provided in SEQ ID NO: 307, with the corresponding amino acid sequence being provided in SEQ ID NO: 308. Further studies led to the isolation of a splice variant of B311D. The B311D clone of SEQ ID NO: 316 was sequenced and a XhoI/NotI fragment from this clone was gel purified and 32P-cDTP labeled by random priming for use as a probe for further screening to obtain additional B311D gene sequence. Two fractions of a human breast tumor cDNA bacterial library were screened using standard techniques. One of the clones isolated in this manner yielded additional sequence which includes a poly A+ tail. The determined cDNA sequence of this clone (referred to as B311D_BT1_1A) is provided in SEQ ID NO: 317. The sequences of SEQ ID NO: 316 and 317 were found to share identity over a 464 bp region, with the sequences diverging near the poly A+ sequence of SEQ ID NO: 317.

Subsequent studies identified an additional 146 sequences (SEQ ID NOS:142-289), of which 115 appeared to be novel (SEQ ID NOS:142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288 and 291). To the best of the inventors' knowledge none of the previously identified sequences have heretofore been shown to be expressed at a greater level in human breast tumor tissue than in normal breast tissue.

In further studies, several different splice forms of the antigen B11Ag1 (also referred to as B305D) were isolated, with each of the various splice forms containing slightly different versions of the B11Ag1 coding frame. Splice junction sequences define individual exons which, in various patterns and arrangements, make up the various splice forms. Primers were designed to examine the expression pattern of each of the exons using RT-PCR as described below. Each exon was found to show the same expression pattern as the original B11Ag1 clone, with expression being breast tumor-, normal prostate- and normal testis-specific. The determined cDNA sequences for the isolated protein coding exons are provided in SEQ ID NO: 292-298, respectively.

The predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292 and 298 are provided in SEQ ID NO: 299 and 300. Additional studies using rapid amplification of cDNA ends (RACE), a 5' specific primer to one of the splice forms of B11Ag1 provided above and a breast adenocarcinoma, led to the isolation of three additional, related, splice forms referred to as isoforms B11C-15, B11C-8 and B11C-9,16. The determined cDNA sequences for these isoforms are provided in SEQ ID NO: 301-303, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 304-306.

In subsequent studies on B305D isoform A (cDNA sequence provided in SEQ ID NO: 292), the cDNA sequence (provided in SEQ ID NO: 313) was found to contain an additional guanine residue at position 884, leading to a frameshift in the open reading frame. The determined DNA sequence of this ORF is provided in SEQ ID NO: 314. This frameshift generates a protein sequence (provided in SEQ ID NO: 315) of 293 amino acids that contains the C-terminal domain common to the other isoforms of B305D but that differs in the N-terminal region.

EXAMPLE 2

PREPARATION OF B18AG1 DNA FROM HUMAN GENOMIC DNA

This Example illustrates the preparation of B18Ag1 DNA by amplification from human genomic DNA.

B18Ag1 DNA may be prepared from 250 ng human genomic DNA using 20 pmol of B18Ag1 specific primers, 500 pmol dNTPS and 1 unit of *Taq* DNA polymerase (Perkin Elmer, Branchburg, NJ) using the following amplification parameters: 94°C for 30 seconds denaturing, 30 seconds 60°C to 42°C touchdown annealing in 2°C increments every two cycles and 72°C extension for 30 seconds. The last increment (a 42°C annealing temperature) should cycle 25 times. Primers were selected using computer analysis. Primers synthesized were B18Ag1-1, B18Ag1-2, B18Ag1-3, and B18Ag1-4. Primer pairs that may be used are 1+3, 1+4, 2+3, and 2+4.

Following gel electrophoresis, the band corresponding to B18Ag1 DNA may be excised and cloned into a suitable vector.

EXAMPLE 3

PREPARATION OF B18AG1 DNA FROM BREAST TUMOR cDNA

This Example illustrates the preparation of B18Ag1 DNA by amplification from human breast tumor cDNA.

First strand cDNA is synthesized from RNA prepared from human breast tumor tissue in a reaction mixture containing 500 ng poly A+ RNA, 200 pmol of the primer $(T)_{12}AG$ (*i.e.*, TTT TTT TTT TTT AG) (SEQ ID NO: 130), 1X first strand reverse transcriptase buffer, 6.7 mM DTT, 500 mmol dNTPs, and 1 unit AMV or MMLV reverse transcriptase (from any supplier, such as Gibco-BRL (Grand Island, NY)) in a final volume of 30 µl. After first strand synthesis, the cDNA is diluted approximately 25 fold and 1 µl is used for amplification as described in Example 2. While some primer pairs can result in a heterogeneous population of transcripts, the primers B18Ag1-2 (5'ATG GCT ATT TTC GGG GGC TGA CA) (SEQ ID NO: 126) and B18Ag1-3 (5'CCG GTA TCT CCT CGT GGG TAT T) (SEQ ID NO: 127) yield a single 151 bp amplification product.

EXAMPLE 4

IDENTIFICATION OF B-CELL AND T-CELL EPITOPES OF B18AG1

This Example illustrates the identification of B18Ag1 epitopes.

The B18Ag1 sequence can be screened using a variety of computer algorithms. To determine B-cell epitopes, the sequence can be screened for hydrophobicity and hydrophilicity values using the method of Hopp, *Prog. Clin. Biol. Res. 172B*:367-77 (1985) or, alternatively, Cease et al., *J. Exp. Med. 164*:1779-84 (1986) or Spouge et al., *J. Immunol. 138*:204-12 (1987). Additional Class II MHC (antibody or B-cell) epitopes can be predicted using programs such as AMPHI (*e.g.*, Margalit et al., *J.*

Immunol. 138:2213 (1987)) or the methods of Rothbard and Taylor (*e.g.*, *EMBO J.* 7:93 (1988)).

Once peptides (15-20 amino acids long) are identified using these techniques, individual peptides can be synthesized using automated peptide synthesis equipment (available from manufacturers such as Perkin Elmer/Applied Biosystems Division, Foster City, CA) and techniques such as Merrifield synthesis. Following synthesis, the peptides can used to screen sera harvested from either normal or breast cancer patients to determine whether patients with breast cancer possess antibodies reactive with the peptides. Presence of such antibodies in breast cancer patient would confirm the immunogenicity of the specific B-cell epitope in question. The peptides can also be tested for their ability to generate a serologic or humoral immune in animals (mice, rats, rabbits, chimps etc.) following immunization *in vivo*. Generation of a peptide-specific antiserum following such immunization further confirms the immunogenicity of the specific B-cell epitope in question.

To identify T-cell epitopes, the B18Ag1 sequence can be screened using different computer algorithms which are useful in identifying 8-10 amino acid motifs within the B18Ag1 sequence which are capable of binding to HLA Class I MHC molecules. (*see*, *e.g.*, Rammensee et al., *Immunogenetics 41*:178-228 (1995)). Following synthesis such peptides can be tested for their ability to bind to class I MHC using standard binding assays (*e.g.*, Sette et al., *J. Immunol. 153*:5586-92 (1994)) and more importantly can be tested for their ability to generate antigen reactive cytotoxic T-cells following *in vitro* stimulation of patient or normal peripheral mononuclear cells using, for example, the methods of Bakker et al., *Cancer Res. 55*:5330-34 (1995); Visseren et al., *J. Immunol. 154*:3991-98 (1995); Kawakami et al., *J. Immunol. 154*:3961-68 (1995); and Kast et al., *J. Immunol. 152*:3904-12 (1994). Successful *in vitro* generation of T-cells capable of killing autologous (bearing the same Class I MHC molecules) tumor cells following *in vitro* peptide stimulation further confirms the immunogenicity of the B18Ag1 antigen. Furthermore, such peptides may be used to generate murine peptide and B18Ag1 reactive cytotoxic T-cells following *in vivo* immunization in mice rendered

transgenic for expression of a particular human MHC Class I haplotype (Vitiello et al., *J. Exp. Med. 173*:1007-15 (1991).

A representative list of predicted B18Ag1 B-cell and T-cell epitopes, broken down according to predicted HLA Class I MHC binding antigen, is shown below:

Predicted Th Motifs (B-cell epitopes) (SEQ ID NOS.: 131-133)

SSGGRTFDDFHRYLLVGI

QGAAQKPINLSKXIEVVQGHDE

SPGVFLEHLQEAYRIYTPFDLSA

Predicted HLA A2.1 Motifs (T-cell epitopes) (SEQ ID NOS.: 134-140)

YLLVGIQGA

GAAQKPINL

NLSKXIEVV

EVVQGHDES

HLQEAYRIY

NLAFVAQAA

FVAQAAPDS

EXAMPLE 5

IDENTIFICATION OF T-CELL EPITOPES OF B11AG1

This Example illustrates the identification of B11Ag1 (also referred to as B305D) epitopes. Four peptides, referred to as B11-8, B11-1, B11-5 and B11-12 (SEQ ID NO: 309-312, respectfully) were derived from the B11Ag1 gene.

Human CD8 T cells were primed *in vitro* to the peptide B11-8 using dendritic cells according to the protocol of Van Tsai et al. (*Critical Reviews in Immunology 18*:65-75, 1998). The resulting CD8 T cell cultures were tested for their ability to recognize the B11-8 peptide or a negative control peptide, presented by the B-LCL line, JY. Briefly, T cells were incubated with autologous monocytes in the presence of 10 ug/ml peptide, 10 ng/ml IL-7 and 10 ug/ml IL-2, and assayed for their ability to

specifically lyse target cells in a standard 51-Cr release assay. As shown in Fig. 22, the bulk culture line demonstrated strong recognition of the B11-8 peptide with weaker recognition of the peptide B11-1.

A clone from this CTL line was isolated following rapid expansion using the monoclonal antibody OKT3 and human IL-2. As shown in Fig. 23, this clone (referred to as A1), in addition to being able to recognize specific peptide, recognized JY LCL transduced with the B11Ag1 gene. This data demonstrates that B11-8 is a naturally processed epitope of the B11Ag1 gene. In addition these T cells were further found to recognize and lyse, in an HLA-A2 restricted manner, an established tumor cell line naturally expressing B11Ag1 (Fig. 24). The T cells strongly recognize a lung adenocarcinoma (LT-140-22) naturally expressing B11Ag1 transduced with HLA-A2, as well as an A2+ breast carcinoma (CAMA-1) transduced with B11Ag1, but not untransduced lines or another negative tumor line (SW620).

These data clearly demonstrate that these human T cells recognize not only B11-specific peptides but also transduced cells, as well as naturally expressing tumor lines.

CTL lines raised against the antigens B11-5 and B11-12, using the procedures described above, were found to recognize corresponding peptide-coated targets.

Example 6

CHARACTERIZATION OF BREAST TUMOR GENES DISCOVERED BY DIFFERENTIAL DISPLAY PCR

The specificity and sensitivity of the breast tumor genes discovered by differential display PCR were determined using RT-PCR. This procedure enabled the rapid evaluation of breast tumor gene mRNA expression semiquantitatively without using large amounts of RNA. Using gene specific primers, mRNA expression levels in a variety of tissues were examined, including 8 breast tumors, 5 normal breasts, 2 prostate tumors, 2 colon tumors, 1 lung tumor, and 14 other normal adult human tissues, including normal prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach and testes.

To ensure the semiquantitative nature of the RT-PCR, β-actin was used as internal control for each of the tissues examined. Serial dilutions of the first strand cDNAs were prepared and RT-PCR assays performed using β-actin specific primers. A dilution was then selected that enabled the linear range amplification of β-actin template, and which was sensitive enough to reflect the difference in the initial copy number. Using this condition, the β-actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative result when using first strand cDNA that was prepared without adding reverse transcriptase.

Using gene specific primers, the mRNA expression levels were determined in a variety of tissues. To date, 38 genes have been successfully examined by RT-PCR, five of which exhibit good specificity and sensitivity for breast tumors (B15AG-1, B31GA1b, B38GA2a, B11A1a and B18AG1a). Figures 21A and 21B depict the results for three of these genes: B15AG-1 (SEQ ID NO:27), B31GA1b (SEQ ID NO:148) and B38GA2a (SEQ ID NO. 157). Table I summarizes the expression level of all the genes tested in normal breast tissue and breast tumors, and also in other tissues.

TABLE I

Percentage of Breast Cancer Antigens that are Expressed in Various Tissues

Breast Tissues	Over-expressed in Breast Tumors	84%
	Equally Expressed in Normals and Tumor	16%
Other Tissues	Over-expressed in Breast Tumors but not in any Normal Tissues	9%
	Over-expressed in Breast Tumors but Expressed in Some Normal Tissues	30%
	Over-expressed in Breast Tumors but Equally Expressed in All Other Tissues	61%

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purpose of illustration, various modifications may be made without deviating from the spirit and scope of the invention.

CLAIMS

1. An isolated polypeptide, comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

(c) complements of sequences of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences.

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NOs: 299, 300, 304-306, 308 and 315.

4. An isolated polynucleotide encoding at least 15 amino acid

residues of a protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing sequences.

6. An isolated polynucleotide, comprising a sequence recited in any one of SEQ ID Nos: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317.

7. An isolated polynucleotide, comprising a sequence that hybridizes to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions.

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector, comprising a polynucleotide according to any one of claims claim 4-8.

10. A host cell transformed or transfected with an expression vector according to claim 9.

11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences.

12. A fusion protein, comprising at least one polypeptide according to claim 1.

13. A fusion protein according to claim 12, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

14. A fusion protein according to claim 12, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

15. A fusion protein according to claim 12, wherein the fusion protein comprises an affinity tag.

16. An isolated polynucleotide encoding a fusion protein according to claim 12.

17. A pharmaceutical composition, comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:

(a) a polypeptide according to claim 1;

(b) a polynucleotide according to claim 4;

(c) an antibody according to claim 11;

(d) a fusion protein according to claim 12; and

(e) a polynucleotide according to claim 16.

18. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

(a) a polypeptide according to claim 1;

(b) a polynucleotide according to claim 4;

(c) an antibody according to claim 11;

(d) a fusion protein according to claim 12; and

(e) a polynucleotide according to claim 16.

19. A vaccine according to claim 18, wherein the immunostimulant is an adjuvant.

20. A vaccine according to any claim 18, wherein the immunostimulant induces a predominantly Type I response.

21. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 17.

22. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to

claim 18.

23. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.

25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs:_ 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

(c) complements of sequences of (i) or (ii);

in combination with an immunostimulant.

26. A vaccine according to claim 25, wherein the immunostimulant is an adjuvant.

27. A vaccine according to claim 25, wherein the immunostimulant induces a predominantly Type I response.

28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.

29. A method for inhibiting the development of a cancer in a patient,

comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

(b) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

(c) complements of sequences encoded by a polynucleotide recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

and thereby inhibiting the development of a cancer in the patient.

30. A method according to claim 29, wherein the antigen-presenting cell is a dendritic cell.

31. A method according to any one of claims 21, 22 and 29, wherein the cancer is breast cancer.

32. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317; and

(ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the antigen from the sample.

33. A method according to claim 32, wherein the biological sample is

blood or a fraction thereof.

34. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 32.

35. A method for stimulating and/or expanding T cells specific for a protein, comprising contacting T cells with at least one component selected from the group consisting of:

(a) polypeptides comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) sequences recited in SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

(ii) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

(iii) complements of sequences of (i) or (ii);

(b) polynucleotides encoding a polypeptide of (a); and

(c) antigen presenting cells that express a polypeptide of (a);

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

36. An isolated T cell population, comprising T cells prepared according to the method of claim 35.

37. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 36.

38. A method for inhibiting the development of a cancer in a patient,

comprising the steps of:

(a) incubating $CD4^+$ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(1) sequences recited in SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

(2) sequences that hybridize to a sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

(3) complements of sequences of (1) or (2);

(ii) polynucleotides encoding a polypeptide of (i); and

(iii) antigen presenting cells that expresses a polypeptide of (i);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

39. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating $CD4^+$ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:

(i) polypeptides comprising at least an immunogenic portion of a protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(1) sequences recited in SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317;

(2) sequences that hybridize to a sequence recited in

any one of SEQ ID NOs:_ 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 under moderately stringent conditions; and

(3) complements of sequences of (1) or (2);

(ii) polynucleotides encoding a polypeptide of (i); and

(iii) antigen presenting cells that express a polypeptide of (i);

such that T cells proliferate;

(b) cloning at least one proliferated cell to provide cloned T cells; and

(c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

40. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with a binding agent that binds to a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent; and

(c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

41. A method according to claim 40, wherein the binding agent is an antibody.

42. A method according to claim 43, wherein the antibody is a monoclonal antibody.

43. A method according to claim 40, wherein the cancer is breast

cancer.

44. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

45. A method according to claim 44, wherein the binding agent is an antibody.

46. A method according to claim 45, wherein the antibody is a monoclonal antibody.

47. A method according to claim 44, wherein the cancer is a breast cancer.

48. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence

recited in any one of SEQ ID NO: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

49. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

50. A method according to claim 48, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

51. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 1, 3-26, 28-86, 142-253, 255-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotide sequences;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

52. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

53. A method according to claim 51, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

54. A diagnostic kit, comprising:

(a) one or more antibodies according to claim 11; and

(b) a detection reagent comprising a reporter group.

55. A kit according to claim 54, wherein the antibodies are immobilized on a solid support.

56. A kit according to claim 54, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

57. A kit according to claim 54, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

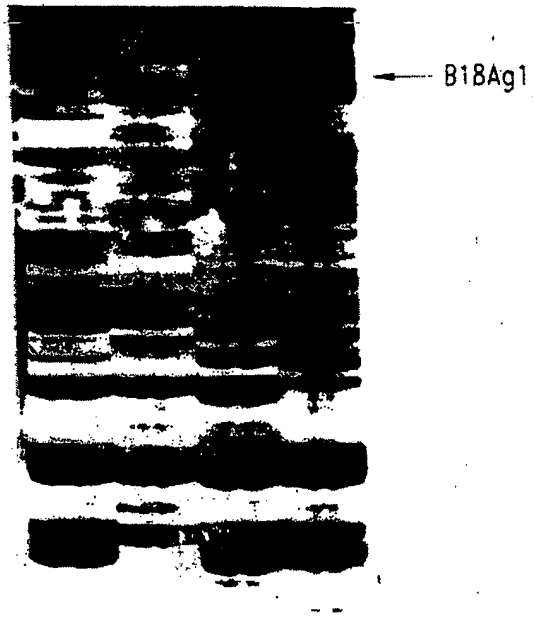
58. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317 or a complement of any of the foregoing polynucleotides.

59. A oligonucleotide according to claim 58, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID Nos: 1, 3-26, 28-77, 142, 143, 146-152, 154-166, 168-176, 178-192, 194-198, 200-204, 206, 207, 209-214, 216, 218, 219, 221-240, 243-245, 247, 250, 251, 253, 255, 257-266, 268, 269, 271-273, 275, 276, 278, 280, 281, 284, 288, 291-298, 301-303, 307, 313, 314, 316 and 317.

60. A diagnostic kit, comprising:

(a) an oligonucleotide according to claim 59; and

(b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.


cDNA PREPARED FROM NORMAL BREAST TISSUE FROM THE SAME PATIENT
cDNA PREPARED FROM BREAST TUMOR
B18Ag1

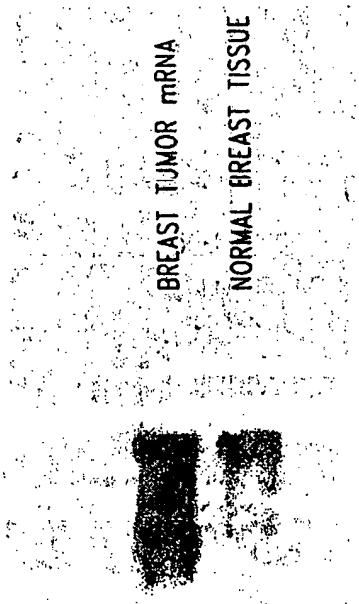
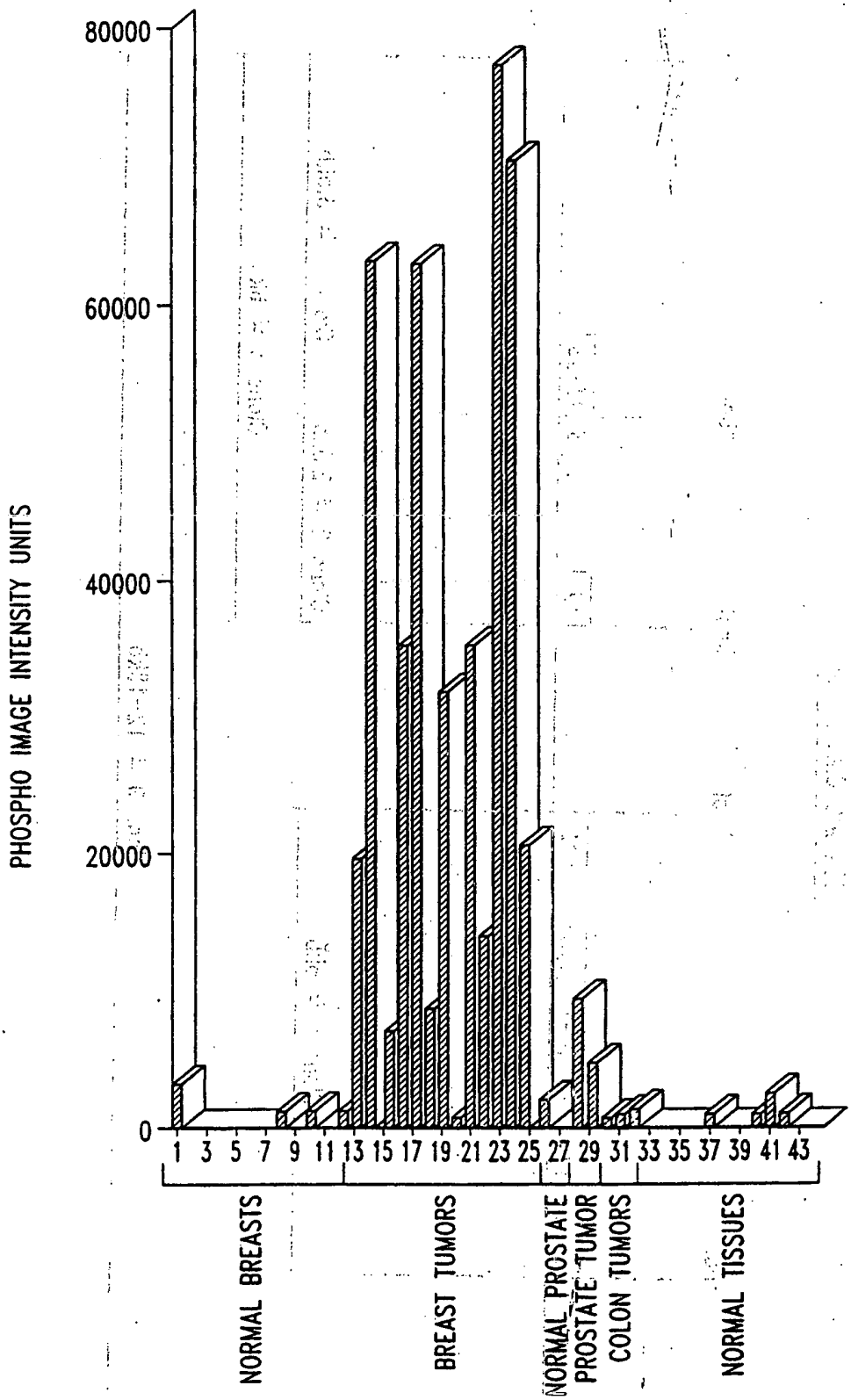


Fig. 2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60000
40000
20000
0
PHOSPHO IMAGE INTENSITY UNITS
1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37 39 41 43
NORMAL BREASTS
BREAST TUMORS
NORMAL PROSTATE
PROSTATE TUMOR
COLON TUMORS
NORMAL TISSUES

Fig. 3

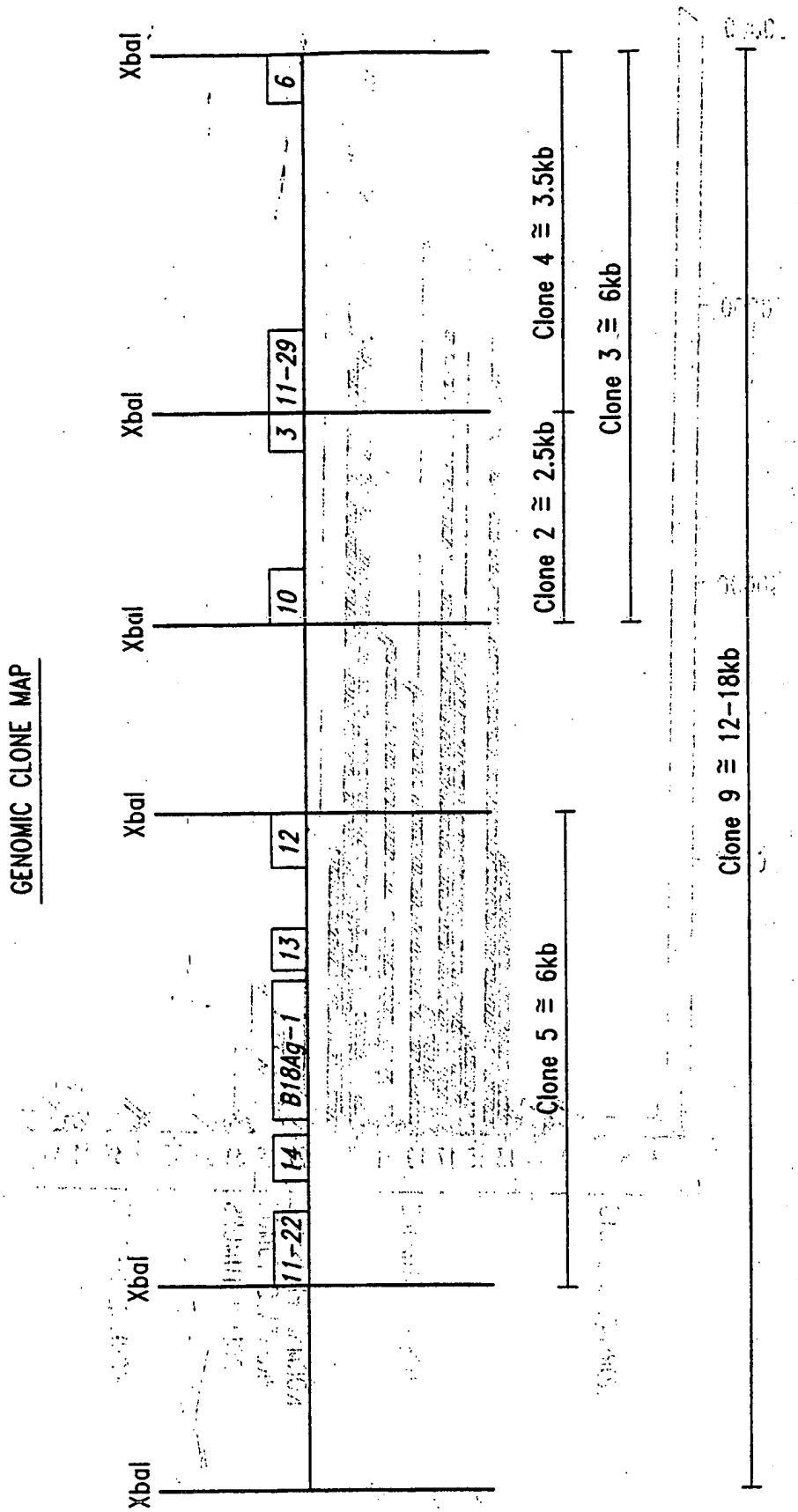
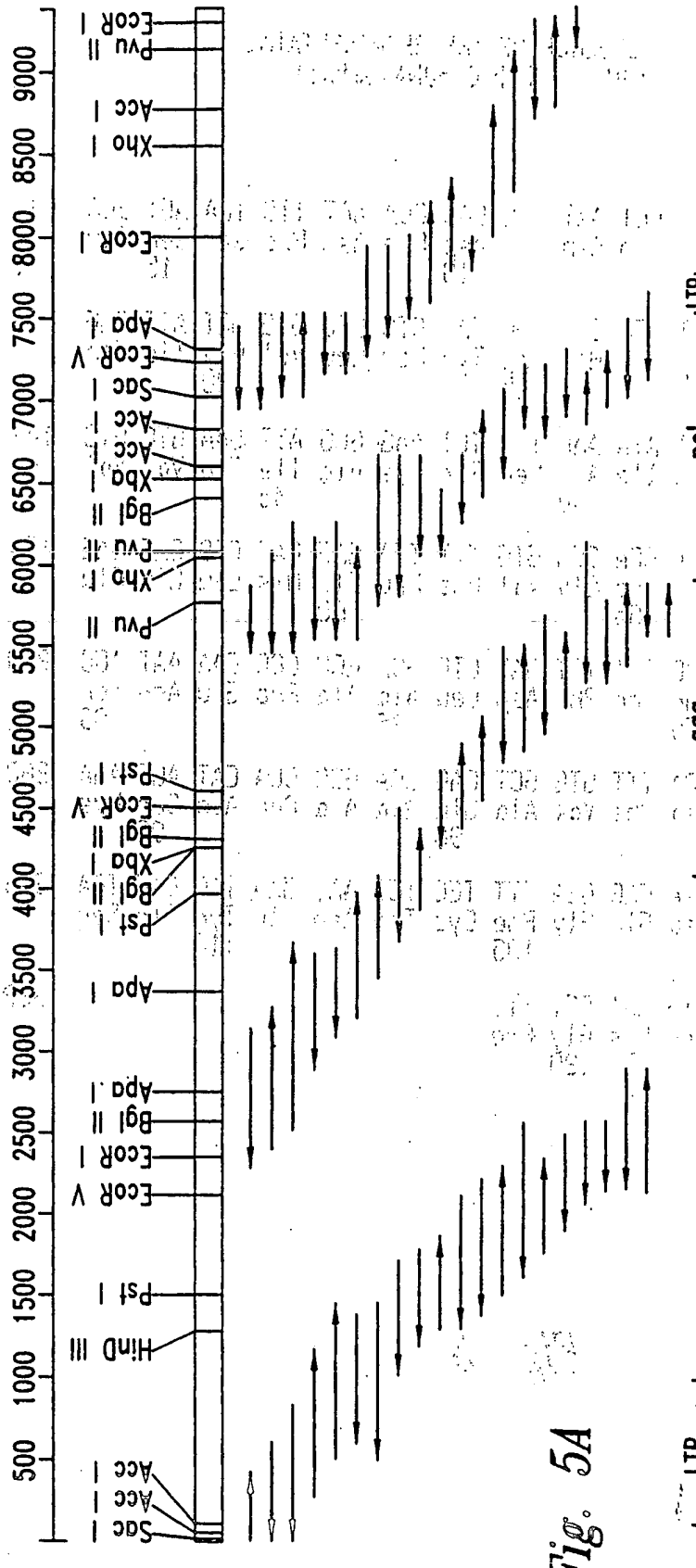


Fig. 4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9000
Sac I
Acc I
Acc I
Hind III
Pst I
EcoR V
EcoR I
Bgl II
Apa I
Pst I
Bgl II
Xba I
Bgl II
EcoR V
Pst I
Pvu II
Xho I
Pvu II
Bgl II
Xba I
Acc I
Acc I
Sac I
EcoR V
Apa I
EcoR I
Xho I
Acc I
Pvu II
EcoR I

Fig. 5A

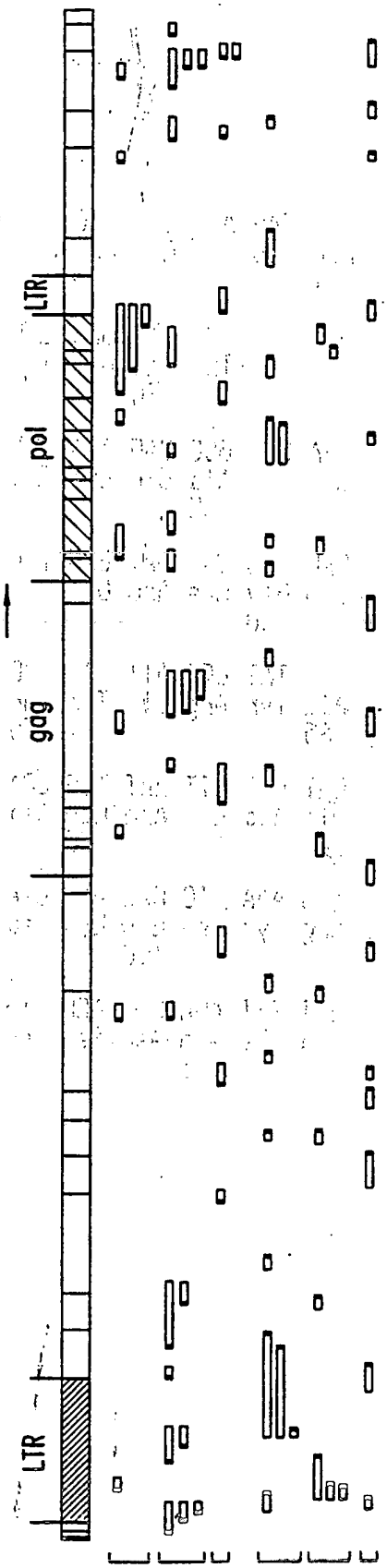
LTR
gag
pol
LTR
1
2
3
4
5
6

Fig. 5B

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE BREAST-TUMOR SPECIFIC cDNA B18Ag1

```
TTA GAG ACC CAA TTG GGA CCT AAT TGG GAC CCA AAT TTC TCA AGT GGA   48
Leu Glu Thr Gln Leu Gly Pro Asn Trp Asp Pro Asn Phe Ser Ser Gly
  1               5                  10                  15

GGG AGA ACT TTT GAC GAT TTC CAC CGG TAT CTC CTC GTG GGT ATT CAG   96
Gly Arg Thr Phe Asp Asp Phe His Arg Tyr Leu Leu Val Gly Ile Gln
            20                  25                  30

GGA GCT GCC CAG AAA CCT ATA AAC TTG TCT AAG GCG ATT GAA GTC GTC  144
Gly Ala Ala Gln Lys Pro Ile Asn Leu Ser Lys Ala Ile Glu Val Val
        35                  40                  45

CAG GGG CAT GAT GAG TCA CCA GGA GTG TTT TTA GAG CAC CTC CAG GAG  192
Gln Gly His Asp Glu Ser Pro Gly Val Phe Leu Glu His Leu Gln Glu
    50                  55                  60

GCT TAT CGG ATT TAC ACC CCT TTT GAC CTG GCA GCC CCC GAA AAT AGC  240
Ala Tyr Arg Ile Tyr Thr Pro Phe Asp Leu Ala Ala Pro Glu Asn Ser
65                  70                  75                  80

CAT GCT CTT AAT TTG GCA TTT GTG GCT CAG GCA GCC CCA GAT AGT AAA  288
His Ala Leu Asn Leu Ala Phe Val Ala Gln Ala Ala Pro Asp Ser Lys
                85                  90                  95

AGG AAA CTC CAA AAA CTA GAG GGA TTT TGC TGG AAT GAA TAC CAG TCA  336
Arg Lys Leu Gln Lys Leu Glu Gly Phe Cys Trp Asn Glu Tyr Gln Ser
            100                 105                 110

GCT TTT AGA GAT AGC CTA AAA GGT TTT                             363
Ala Phe Arg Asp Ser Leu Lys Gly Phe
        115                 120
```

Fig. 6

NUCLEOTIDE SEQUCNE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B17Ag1

GC TGGGCACAGT GGCTCATACC TGTAATCCTG ACCGTTTCAG AGGCTCAGGT 60

CG CTTGAGCCCA AGATTTCAAG ACTAGTCTGG GTAACATAGT GAGACCCTAT 120

AA AAATAAAAAA ATGAGCCTGG TGTAGTGGCA CACACCAGCT GAGGAGGGAG 180

CT AGGAGA 196

Fig. 7

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B17Ag2

```
GC TTGGGGGCTC TGACTAGAAA TTCAAGGAAC CTGGGATTCA AGTCCAACTG      60
AC TTACACTGTG GNCTCCAATA AACTGCTTCT TTCCTATTCC CTCTCTATTA     120
AA GGAAAACGAT GTCTGTGTAT AGCCAAGTCA GNTATCCTAA AAGGAGATAC     180
AT TAAATATCAG AATGTAAAAC CTGGGAACCA GGTTCCCAGC CTGGGATTAA     240
CA AGAAGACTGA ACAGTACTAC TGTGAAAAGC CCGAAGNGGC AATATGTTCA     300
TT GAAGGATGGC TGGGAGAATG AATGCTCTGT CCCCCAGTCC CAAGCTCACT     360
CT CCTTTATAGC CTAGGAGA                                       388
```

Fig. 8

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B13Ag2a

GC CTATAATCAT GTTTCTCATT ATTTTCACAT TTTATTAACC AATTTCTGTT	60
AA AATATGAGGG AAATATATGA AACAGGGAGG CAATGTTCAG ATAATTGATC	120
TG ATTTCTACAT CAGATGCTCT TTCCTTTCCT GTTTATTTCC TTTTTATTTC	180
GG TCGAATGTAA TAGCTTTGTT TCAAGAGAGA GTTTTGGCAG TTTCTGTAGC	240
CT GCTCATGTCT CCAGGCATCT ATTTGCACTT TAGGAGGTGT CGTGGGAGAC	300
CT ATTTTTTCCA TATTTGGGCA ACTACTA	337

Fig. 9

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B13Ag1b

GC CATACAGTGC CTTTCCATTT ATTTAACCCC CACCTGAACG GCATAAACTG	60
GC TGGTGTTTTT TACTGTAAAC AATAAGGAGA CTTTGCTCTT CATTTAAACC	120
AT TTCATATTTT ACGCTCGAGG GTTTTTACCG GTTCCTTTTT ACACTCCTTA	180
TT TAAGTCGTTT GGAACAAGAT ATTTTTTCTT TCCTGGCAGC TTTTAACATT	240
TT TGTGTCTGGG GGACTGCTGG TCACTGTTTC TCACAGTTGC AAATCAAGGC	300
CC AAGAAAAAAA AATTTTTTTG TTTTATTTGA AACTGGACCG GATAAACGGT	360
CG GCTGCTGTAT ATAGTTTTAA ATGGTTTATT GCACCTCCTT AAGTTGCACT	420
GG GGGGNTTTTG NATAGAAAGT NTTTANTCAC ANAGTCACAG GGACTTTTNT	480
NA CTGAGCTAAA AAGGGCTGNT TTTCGGGTGG GGGCAGATGA AGGCTCACAG	540
TC TCTTAGAGGG GGGAACTNCT A	571

Fig. 10

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B13Ag1a

```
TA ATAACTTAAA TATATTTTGA TCACCCACTG GGGTGATAAG ACAATAGATA      60

TT TCCAAAAACC ATAAAACCAA AGTATCATAC CAAACCAAAT TCATACTGCT     120

CC GCACTGAAAC TTCACCTTCT AACTGTCTAC CTAACCAAAT TCTACCCTTC     180

GG TGCGTGCTCA CTACTCTTTT TTTTTTTTTT TTTNTTTTGG AGATGGAGTC     240

CA GCCCAGGGGT GGAGTACAAT GGCACAACCT CAGCTCACTG NAACCTCCGC     300

TT CATGAGATTC TCCTGNTTCA GCCTTCCCAG TAGCTGGGAC TACAGGTGTG     360

TG CCTGGNTAAT CTTTTTTTNGT TTTNGGGTAG AGATGGGGGT TTTACATGTT     420

TG GTNTCGAACT CCTGACCTCA AGTGATCCAC CCACCTCAGG CTCCCAAAGT     480

TA CAGACATGAG CCACTGNGCC CAGNCCTGGT GCATGCTCAC TTCTCTAGGC     540

                                                              548
```

Fig. 11

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B11Ag1

TG CACATGCAGA ATATTCTATC GGTACTTCAG CTATTACTCA TTTTGATGGC	60
AG CCTATCCTCA AGATGAGTAT TTAGAAAGAA TTGATTTAGC GATAGACCAA	120
GC ACTCTGACTA CACGAAATTG TTCAGATGTG ATGGATTTAT GACAGTTGAT	180
GA GATTATTAAG TGATTATTTT AAAGGGAATC CATTAATTCC AGAATATCTT	240
TC AAGATGATAT AGAAATAGAA CAGAAAGAGA CTACAAATGA AGATGTATCA	300
TA TTGAAGAGCC TATAGTAGAA AATGAATTAG CTGCATTTAT TAGCCTTACA	360
TT TTCCTGATGA ATCTTATATT CAGCCATCGA CATAGCATTA CCTGATGGGC	420
GA ATAATAGAAA CTGGGTGCGG GGCTATTGAT GAATTCATCC NCAGTAAATT	480
AC AAAATATAAC TCGATTGCAT TTGGATGATG GAATACTAAA TCTGGCAAAA	540
GG AGCTACTAGT AACCTCTCTT TTTGAGATGC AAAATTTTCT TTTAGGGTTT	600
CT ACTTTACGGA TATTGGAGCA TAACGGGA	638

Fig. 12

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE BREAST-TUMOR SPECIFIC cDNA B3CA3c

ACTGATGGAT GTCGCCGGAG GCGAGGGGCC TTATCTGATG CTCGGCTGCC TGTTCGTGAT 60

GTGCGCGGCG ATTGGGCTGT TTATCTCAAA CACCGCCACG GCGGTGCTGA TGGCGCCTAT 120

TGCCTTAGCG GCGGCGAAGT CAATGGGCGT CTCACCCTAT CCTTTTGCCA TGGTGGTGGC 180

GATGGCGGCT TCGGCGGCGT TTATGACCCC GGTCTCCTCG CCGGTTAACA CCCTGGTGCT 240

TGGCCCTGGC AAGTACTCAT TTAGCGATTT TGTCAAAATA GGCGTG 286

Fig. 13

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B9CG1

```
AG CAGCCCCTTC TTCTCAATTT CATCTGTCAC TACCCTGGTG TAGTATCTCA      60

CA TTTTTATAGC CTCCTCCCTG GTCTGTCTTT TGATTTTCCT GCCTGTAATC     120

AC ATAACTGCAA GTAAACATTT CTAAAGTGTG GTTATGCTCA TGTCACTCCT     180

AA ATAGTTTCCA TTACCGTCTT AATAAAATTC GGATTTGTTC TTTNCTATTN     240

CA CCTATGACCG AA                                             262
```

Fig. 14

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B9CG3

AG CAAAGCCAGT GGTTTGAGCT CTCTACTGTG TAAACTCCTA AACCAAGGCC 60

TA AATGGTGGCA GGATTTTTAT TATAAACATG TACCCATGCA AATTTCCTAT 120

GA TATATTCTTC TACATTTAAA CAATAAAAAT AATCTATTTT TAAAAGCCTA 180

AG TTAGGTAAGA GTGTTTAATG AGAGGGTATA AGGTATAAAT CACCAGTCAA 240

TG CCTATGACCG A 261

Fig. 15

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA-B2CA2

GG GCATGGACGC AGACGCCTGA CGTTTGGCTG AAAATCTTTC ATTGATTCGT 60

AT AGGAAAATTC CCAAAGAGGG AATGTCCTGT TGCTCGCCAG TTTTTNTGTT 120

GG ANAAGGCAAN GAGCTCTTCA GACTATTGGN ATTNTCGTTC GGTCTTCTGC 180

CG NCTTGCNANG ATCTTCAT 208

Fig. 16

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE BREAST-TUMOR SPECIFIC cDNA B3CA1

GG GCATGGACGC AGACGCCTGA CGTTTGGCTG AAAATCTTTC ATTGATTCGT 60

AT AGGAAAATTC CCAAAGAGGG AATGTCCTGT TGCTCGCCAG TTTTTNTGTT 120

GG ANAAGGCAAN GAGCTCTTCA GACTATTGGN ATTNTCGTTC GGTCTTCTGC 180

CG NCTTGCNANG ATCTTCAT 208

Fig. 17

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B3CA2

```
GG GCATGGACGC AGACGCCTGA CGTTTGGCTG AAAATCTTTC ATTGATTCGT      60

AT AGGAAAATTC CCAAAGAGGG AATGTCCTGT TGCTCGCCAG TTTTTNTGTT     120

GG ANAAGGCAAN GAGCTCTTCA GACTATTGGN ATTNTCGTTC GGTCTTCTGC     180

CG NCTTGCNANG ATCTTCAT                                        208
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Fig. 18

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE BREAST TUMOR SPECIFIC cDNA B3CA3

AG GGAGCAAGGA GAAGGCATGG AGAGGCTCAN GCTGGTCCTG GCCTACGACT 60

CT GTCGCCGGGG ATGGTGGAGA ACTGAAGCGG GACCTCCTCG AGGTCCTCCG 120

TC NCCGTCCAGG AGGAGGGTCT TTCCGTGGTC TNGGAGGAGC GGGGGGAGAA 180

TC ATGGTCNACA TCCC 204

Fig. 19

NUCLEOTIDE SEQUENCE OF THE REPRESENTATIVE
BREAST-TUMOR SPECIFIC cDNA B4CA1

TC AGGAGCGGGT AGAGTGGCAC CATTGAGGGG ATATTCAAAA ATATTATTTT	60
TG ATAGTTGCTG AGTTTTTCTT TGACCCATGA GTTATATTGG AGTTTATTTT	120
CC AATCGCATGG ACATGTTAGA CTTATTTTCT GTTAATGATT NCTATTTTTA	180
GA TTTGAGAAAT TGGTTNTTAT TATATCAATT TTTGGTATTT GTTGAGTTTG	240
GC TTAGTATGTG ACCA	264

Fig. 20

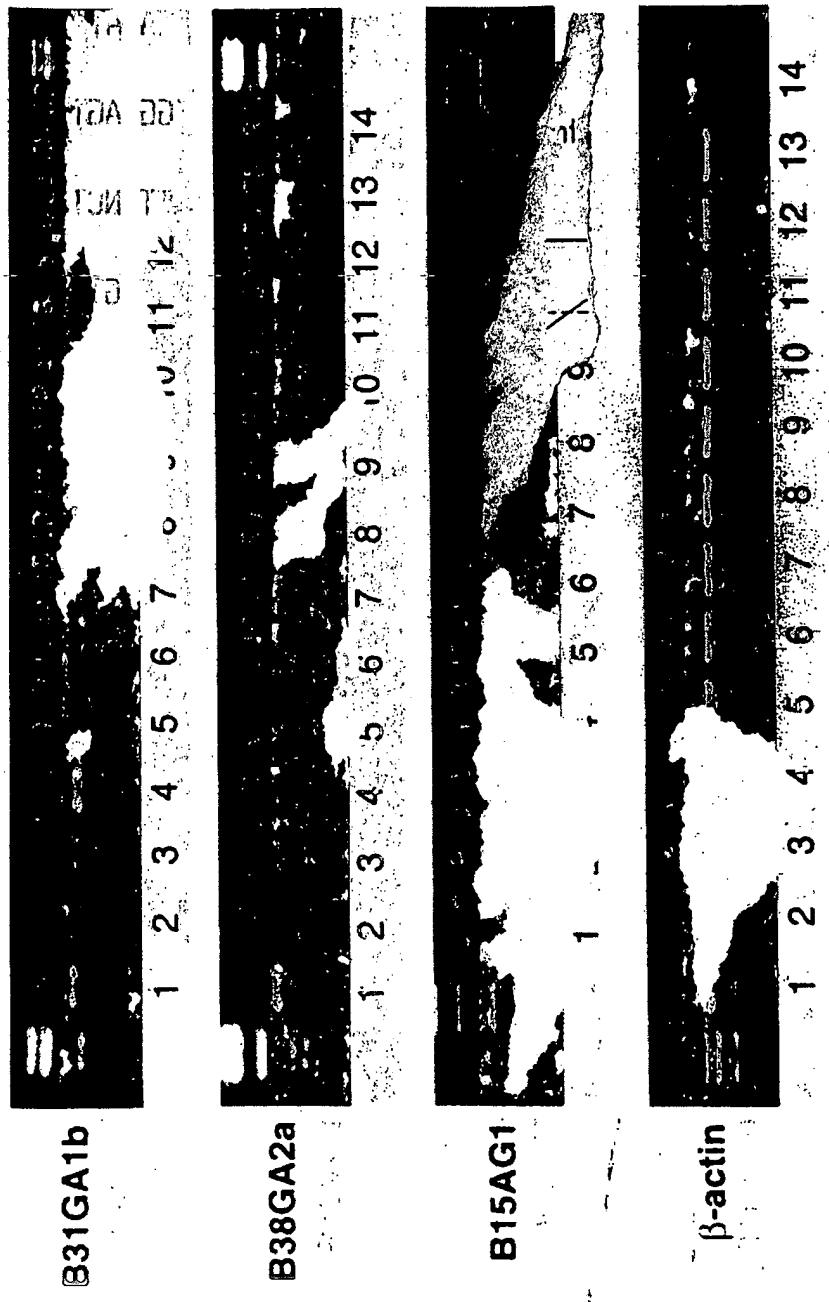


Fig. 21A

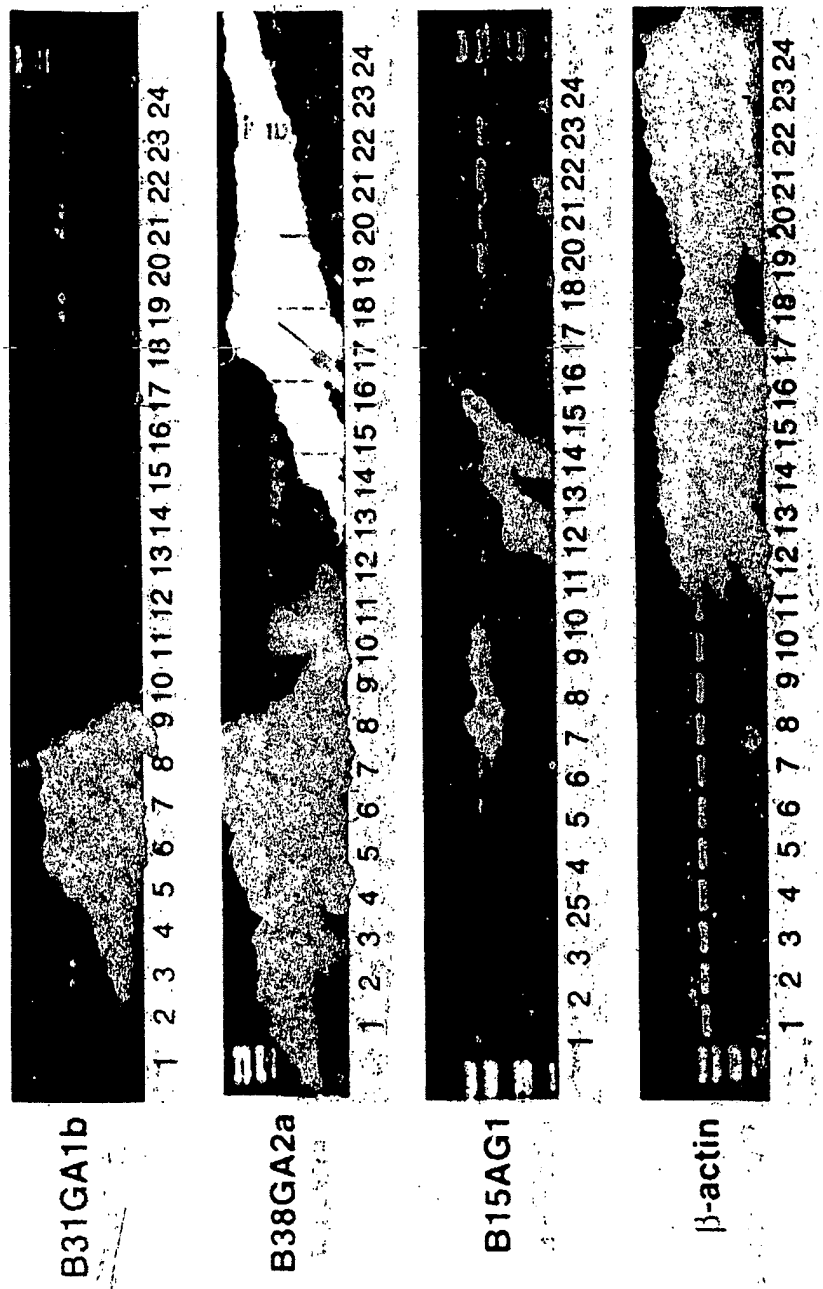
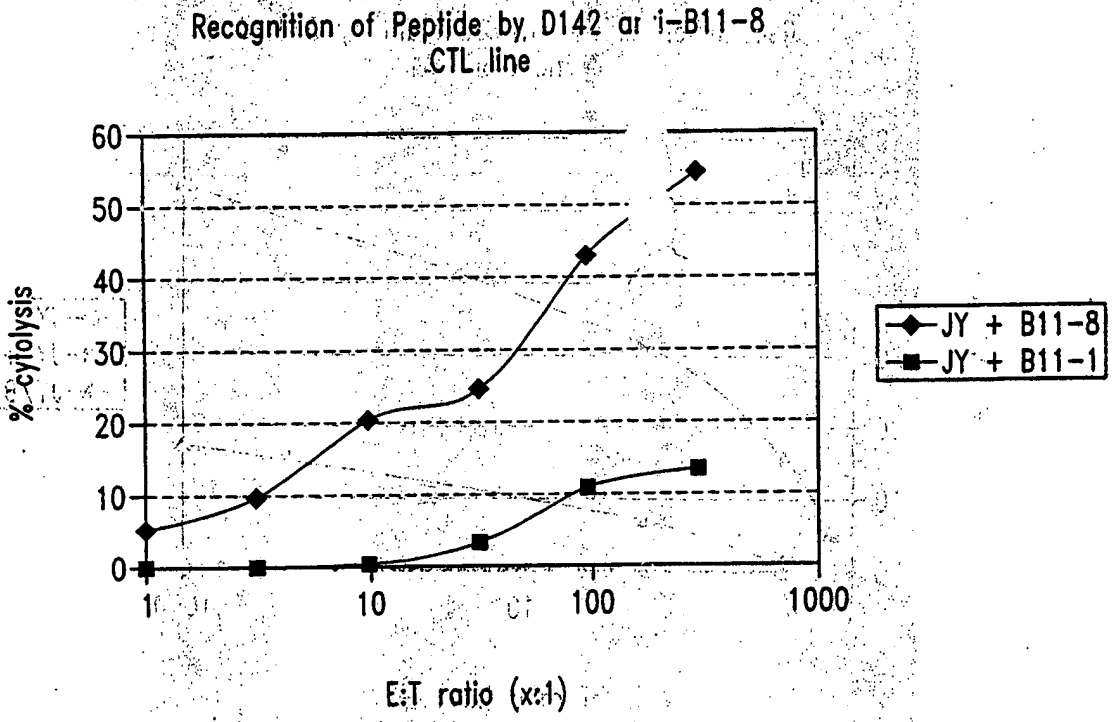


Fig. 21B


Recognition of Peptide by D142 ar i-B11-8 CTL line
% cytolysis
60
50
40
30
20
10
0
1
10
100
1000
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JY + B11-8
JY + B11-1

Fig. 22

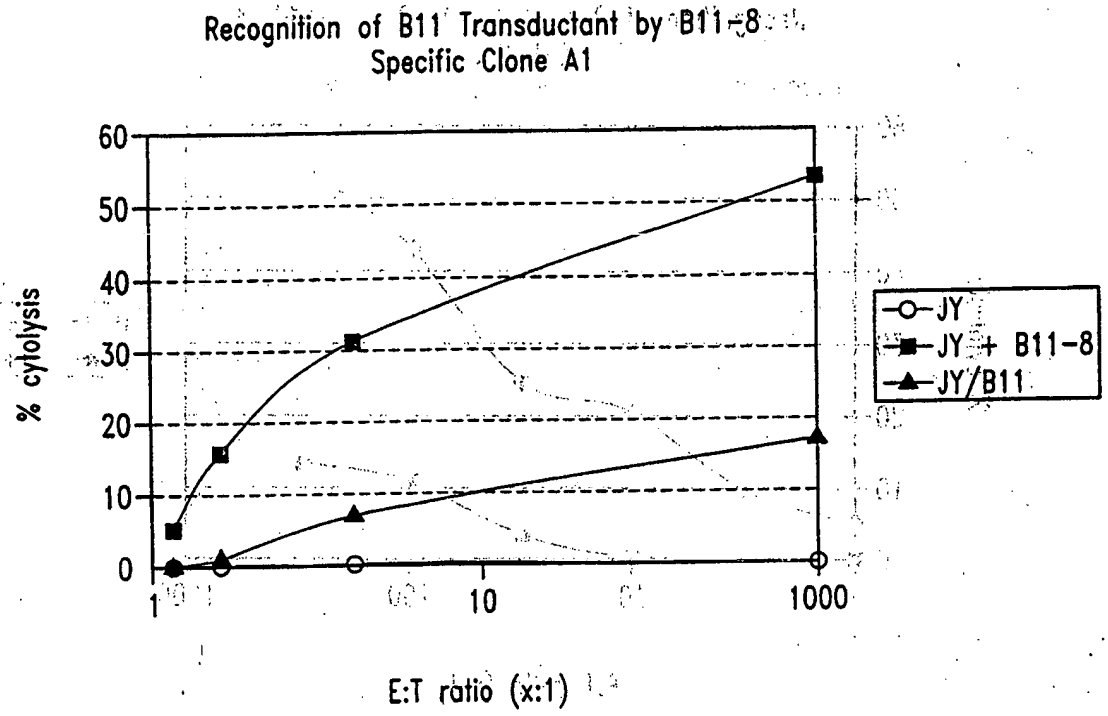
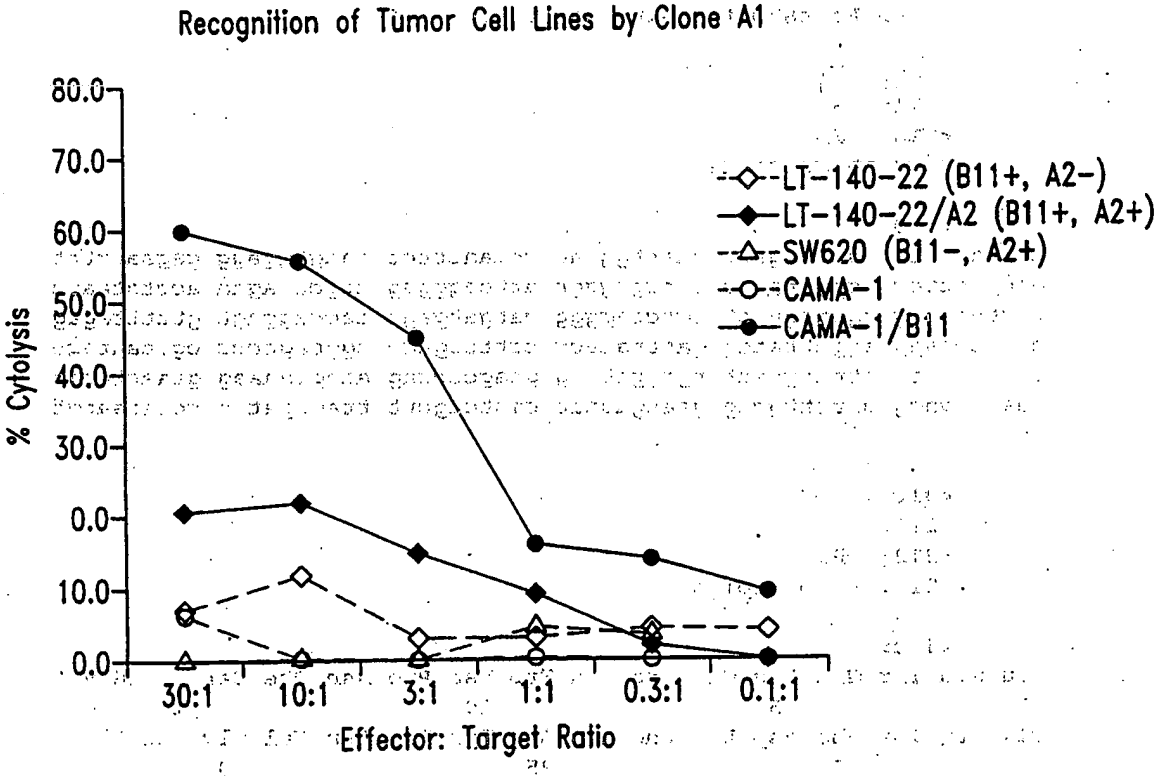


Fig. 23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80.0
70.0
60.0
50.0
40.0
30.0
0.0
10.0
0.0
% Cytolysis
30:1
10:1
3:1
1:1
0.3:1
0.1:1
Effector: Target Ratio
LT-140-22 (B11+, A2-)
LT-140-22/A2 (B11+, A2+)
SW620 (B11-, A2+)
CAMA-1
CAMA-1/B11

Fig 9A

SEQUENCE LISTING

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<120> COMPOSITIONS AND METHODS FOR THE TREATMENT AND DIAGNOSIS OF BREAST CANCER

<130> 210121.41926PC

<140> PCT
<141> 2000-04-07

<160> 317

<170> FastSEQ for Windows Version 3.0

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ttt 363

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Gly Ala Ala Gln Lys Pro Ile Asn Leu Ser Lys Ala Ile Glu Val Val
35 40 45
Gln Gly His Asp Glu Ser Pro Gly Val Phe Leu Glu His Leu Gln Glu
50 55 60
Ala Tyr Arg Ile Tyr Thr Pro Phe Asp Leu Ala Ala Pro Glu Asn Ser
65 70 75 80
His Ala Leu Asn Leu Ala Phe Val Ala Gln Ala Ala Pro Asp Ser Lys
85 90 95
Arg Lys Leu Gln Lys Leu Glu Gly Phe Cys Trp Asn Glu Tyr Gln Ser
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Ala Phe Arg Asp Ser Leu Lys Gly Phe
115 120

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tcttcaaagc ctaacagatc aagcagctct ccggtgcaca acctgcgccc aggtaaatgc 180
caaaaaaggt cctaaaccca gcccaggcca ccgtctccaa gaaaactcac caggagaaaa 240
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gccaggtttc agctgcagat atccctggaa ggaatattcc agattccctg agtagtttcc 300
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acgggtttcc tgttttagtt aggatggccc anntctgacc ccntnatcnt ccccctcngc 840
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tntggantct tgaatnncgg gttttccctt ttaaaccnat ttttttttta nnnccccnan 960
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aggtaacaca catactatct cccaaatacc tacccacaag ctcaacaatt ttaaactgtt 180
aggatcactg gctctaatca ccatgacatg aggtcaccac caaaccatca agcgctaaac 240
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tttnggggan acntggggaa ggtacccccat ttcnttgacc cnncnanaaa acccengtgg 480
ccctttgccc tgattcncnt gggcctttte tcttttcccct tttgggttgt ttaaattccc 540
aatgtccccn gaaccctctc cntnctgccc aaaacctacc taaattnctc nctangnntt 600
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<210> 6
<211> 950
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<220>
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taatatcctt accccatcgg agagcctgag tgagggcgat caattcagcc cttttgtgct 480
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accgg 545

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<212> DNA
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tgacaccaac ttacactgtg gnctccaata aactgcttct ttcctattcc ctctctatta 120
aataaaataa ggaaaacgat gtctgtgtat agccaagtca gntatcctaa aaggagatac 180
taagtgacat taaatatcag aatgtaaaac ctggaacca ggttcccagc ctgggattaa 240
actgacagca agaagactga acagtactac tgtgaaaagc ccgaagnggc aatatgttca 300
ctctaccgtt gaaggatggc tgggagaatg aatgctctgt cccccagtcc caagctcact 360
tactatacct cctttatagc ctaggaga 388

<210> 13
<211> 337
<212> DNA
<213> Homo sapien

<400> 13
tagtagttgc ctataatcat gtttctcatt attttcacat tttattaacc aatttctgtt 60
taccctgaaa aatatgaggg aaatatatga aacagggagg caatgttcag ataattgatc 120
acaagatatg atttctacat cagatgctct ttcctttcct gtttatttcc tttttatttc 180
ggttgtgggg tcgaatgtaa tagctttgtt tcaagagaga gttttggcag tttctgtagc 240
ttctgacact gctcatgtct ccaggcatct atttgcactt taggaggtgt cgtgggagac 300
tgagaggtct atttttttcca tatttgggca actacta 337

<210> 14
<211> 571
<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(571)

<223> n = A,T,C or G

<400> 14

tagtagttgc catacagtgc ctttccattt atttaacccc cacctgaacg gcataaactg 60
agtgttcagc tggtgttttt tactgtaaac aataaggaga ctttgctctt catttaaacc 120
aaaatcatat ttcatatttt acgctcgagg gtttttaccg gttccttttt acactcctta 180
aaacagtttt taagtcgttt ggaacaagat attttttctt tcctggcagc tttaacatt 240
atagcaaatt tgtgtctggg ggactgctgg tcactgtttc tcacagttgc aaatcaaggc 300
atttgcaacc aagaaaaaaa aatttttttg ttttatttga aactggaccg gataaacggt 360
gtttggagcg gctgctgtat atagttttaa atggtttatt gcacctcctt aagttgcact 420
tatgtggggg ggggntttg natagaaagt ntttantcac anagtcacag ggacttttnt 480
cttttggnna ctgagctaaa aagggctgnt tttcgggtgg gggcagatga aggctcacag 540
gaggcctttc tcttagaggg gggaactnct a 571

<210> 15

<211> 548

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(548)

<223> n = A,T,C or G

<400> 15

tatatattta ataacttaaa tatattttga tcacccactg gggtgataag acaatagata 60
taaaagtatt tccaaaaagc ataaaaccaa agtatcatac caaaccaaat tcatactgct 120
tcccccaccc gcactgaaac ttcaccttct aactgtctac ctaaccaaat tctaccctte 180
aagtctttgg tgcgtgctca ctactctttt ttttttttt tttnttttgg agatggagtc 240
tggctgtgca gcccaggggt ggagtacaat ggcacaacct cagctcactg naacctccgc 300
ctcccaggtt catgagattc tcctgnttca gccttcccag tagctgggac tacaggtgtg 360
catcaccatg cctggntaat cttttttngt tttngggtag agatgggggt tttacatgtt 420
ggccaggntg gtntcgaact cctgacctca agtgatccac ccacctcagg ctcccaaagt 480
gctaggatta cagacatgag ccactgngcc cagncctggt gcatgctcac ttctctaggc 540
aactacta 548

<210> 16

<211> 638

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(638)

<223> n = A,T,C or G

<400> 16

ttccgttatg cacatgcaga atattctatc ggtacttcag ctattactca ttttgatggc 60
gcaatccgag cctatcctca agatgagtat ttagaaagaa ttgatttagc gatagaccaa 120
gctggtaagc actctgacta cacgaaattg ttcagatgtg atggatttat gacagttgat 180

ctttggaaga gattattaag tgattatttt aaagggaatc cattaattcc agaatatctt 240
ggtttagctc aagatgatat agaaatagaa cagaaagaga ctacaaatga agatgtatca 300
ccaactgata ttgaagagcc tatagtagaa aatgaattag ctgcatttat tagccttaca 360
catagcgatt ttcctgatga atcttatatt cagccatcga catagcatta cctgatgggc 420
aaccttacga ataatagaaa ctgggtgcgg ggctattgat gaattcatcc ncagtaaatt 480
tggatatnac aaaatataac tcgattgcat ttggatgatg gaatactaaa tctggcaaaa 540
gtaacttttgg agctactagt aacctctctt tttgagatgc aaaatttttct tttagggttt 600
cttattctct actttacgga tattggagca taacggga 638

<210> 17
<211> 286
<212> DNA
<213> Homo sapien

<400> 17
actgatggat gtcgccggag gcgaggggcc ttatctgatg ctcggctgcc tgttcgtgat 60
gtgcgcggcg attgggctgt ttatctcaaa caccgccacg gcggtgctga tggcgcctat 120
tgccttagcg gcggcgaagt caatgggcgt ctcaccctat ccttttgcca tggtggtggc 180
gatggcggct tcggcggcgt ttatgacccc ggtctcctcg ccggttaaca ccctggtgct 240
tggccctggc aagtactcat ttagcgattt tgtcaaaata ggcgtg 286

<210> 18
<211> 262
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(262)
<223> n = A,T,C or G

<400> 18
tcggtcatag cagccccttc ttctcaattt catctgtcac taccctggtg tagtatctca 60
tagccttaca tttttatagc ctcctccctg gtctgtcttt tgattttcct gcctgtaatc 120
catatcacac ataactgcaa gtaaacattt ctaaagtgtg gttatgctca tgtcactcct 180
gtgncaagaa atagtttcca ttaccgtctt aataaaattc ggatttgttc tttnctattn 240
tcactcttca cctatgaccg aa 262

<210> 19
<211> 261
<212> DNA
<213> Homo sapien

<400> 19
tcggtcatag caaagccagt ggtttgagct ctctactgtg taaactccta aaccaaggcc 60
atttatgata aatggtggca ggatttttat tataaacatg tacccatgca aatttcctat 120
aactctgaga tatattcttc tacatttaaa caataaaaat aatctatttt taaaagccta 180
atttgcgtag ttaggtaaga gtgtttaatg agagggtata aggtataaat caccagtcaa 240
cgtttctctg cctatgaccg a 261

<210> 20
<211> 294
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(294)
<223> n = A,T,C or G

<400> 20
tacaacgagg cgacgtcggt aaaatcggac atgaagccac cgctggtctt ttcgtccgag 60
cgataggcgc cggccagcca gcggaacggt tgcccggatg gcgaagcgag cggagttct 120
tcggactgag tatgaatctt gttgtgaaaa tactcgccgc cttcgttcga cgacgtcgcg 180
tcgaaatctt cganctcctt acgatcgaag tcttcgtggg cgacgatcgc ggtcagttcc 240
gccccaccga aatcatggtt gagccggatg ctgnccccga agncctcgtt tgtn 294

<210> 21
<211> 208
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(208)
<223> n = A,T,C or G

<400> 21
ttggtaaagg gcatggacgc agacgcctga cgtttggctg aaaatctttc attgattcgt 60
atcaatgaat aggaaaattc ccaaagaggg aatgtcctgt tgctcgccag ttttntntgtt 120
gttctcatgg anaaggcaan gagctcttca gactattggn attntcgttc ggtcttctgc 180
caactagtcg ncttgcnang atcttcat 208

<210> 22
<211> 287
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(287)
<223> n = A,T,C or G

<400> 22
nccnttgagc tgagtgattg agatntgtaa tggttgtaag ggtgattcag gcggattagg 60
gtggcgggtc acccggcagt gggtctcccg acaggccagc aggatttggg gcaggtacgg 120
ngtgcgcatc gctcgactat atgctatggc aggcgagccg tggaaggngg atcaggtcac 180
ggcgctggag ctttccacgg tccatgnatt gngatggctg ttctaggcgg ctgttgccaa 240
gcgtgatggt acgctggctg gagcattgat ttctggtgcc aaggtgg 287

<210> 23
<211> 204
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(204)
<223> n = A,T,C or G

<400> 23
ttgggtaaag ggagcaagga gaaggcatgg agaggctcan gctggtcctg gcctacgact 60
gggccaagct gtcgccgggg atggtggaga actgaagcgg gacctcctcg aggtcctccg 120
ncgttacttc nccgtccagg aggagggtct ttccgtggtc tnggaggagc ggggggagaa 180
gatnctcctc atggtcnaca tccc 204

<210> 24
<211> 264
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(264)
<223> n = A,T,C or G

<400> 24
tggattggtc aggagcgggt agagtggcac cattgagggg atattcaaaa atattatttt 60
gtcctaaatg atagttgctg agtttttctt tgacccatga gttatattgg agtttatttt 120
ttaactttcc aatcgcatgg acatgttaga cttatttttct gttaatgatt nctattttta 180
ttaaattgga tttgagaaat tggttnttat tatatcaatt tttggtattt gttgagtttg 240
acattatagc ttagtatgtg acca 264

<210> 25
<211> 376
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(376)
<223> n = A,T,C or G

<400> 25
ttacaacgag gggaaactcc gtctctacaa aaattaaaaa attagccagg tgtggtggtg 60
tgcacccgca atcccagcta cttgggaggt tgagacacaa gantcaccta natgtgggag 120
gtcaaggttg catgagtcat gattgtgcca ctgcactcca gcctgggtga cagaccgaga 180
ccctgcctca anaganaang aataggaagt tcagaaatcn tggntgtggn gcccagcaat 240
ctgcatctat ncaacccctg caggcaangc tgatgcagcc tangttcaag agctgctgtt 300
tctggaggca gcagttnggg cttccatcca gtatcacggc cacactcgca cnagccatct 360
gtcctccgtn tgtnac 376

<210> 26
<211> 372
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(372)
<223> n = A,T,C or G

<400> 26
ttacaacgag gggaaactcc gtctctacaa aaattaaaaa attagccagg tgtggtggtg 60
tgcacctgta atcccagcta cttgggcggc tgagacacaa gaaccaccta aatgtgggag 120

ggtcaaggtt gcatgagtca tgatcgcgcc actgcactcc agcctgggtg acagactgag 180
accctgcctc aaaagaaaaa gaataggaag ttcagaaacc ctgggtgtgg ngcccagcaa 240
tctgcattta aacaatccct gcaggcaatg ctgatgcagc ctaagttcaa gagctgctgt 300
tctggaggca gnagtaaggg cttccatcca gcatcacggn caacactgca aaagcacctg 360
tcctcgttgg ta 372

<210> 27
<211> 477
<212> DNA
<213> Homo sapien

<400> 27
ttctgtccac atctacaagt tttatttatt ttgtgggttt tcagggtgac taagtttttc 60
cctacattga aaagagaagt tgctaaaagg tgcacaggaa atcatttttt taagtgaata 120
tgataatatg ggtccgtgct taatacaact gagacatatt tgttctctgt ttttttagag 180
tcacctctta aagtccaatc ccacaatggt gaaaaaaaaa tagaaagtat ttgttctacc 240
tttaaggaga ctgcagggat tctccttgaa aacggagtat ggaatcaatc ttaaataaat 300
atgaaattgg ttggtcttct gggataagaa attcccaact cagtgtgctg aaattcacct 360
gacttttttt gggaaaaaat agtcgaaaat gtcaatttgg tccataaaat acatgttact 420
attaaaagat atttaaagac aaattctttc agagctctaa gattggtgtg gacagaa 477

<210> 28
<211> 438
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(438)
<223> n = A,T,C or G

<400> 28
tctncaacct cttgantgtc aaaaaccttn taggctatct ctaaaagctg actggtattc 60
attccagcaa aatccctcta gtttttggag tttcctttta ctatctgggg ctgcctgagc 120
cacaaatgcc aaattaagag catggctatt ttcgggggct gacaggtcaa aaggggtgta 180
aatccgataa gcctcctgga ggtgctctaa aaacactcct ggtgactcat catgcccctg 240
gacgacttca atcgncttag acaagtttat aggtttctgg gcagctccct gaatacccac 300
gaggagatac cggtggaaat cgtcaaaagt tctccctcca cttgagaaat ttgggtccca 360
attaggtccc aattgggtct ctaatcacta ttcctctagc ttcctcctcc ggnctattgg 420
ttgatgtgag gttgaaga 438

<210> 29
<211> 620
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(620)
<223> n = A,T,C or G

<400> 29
aagagggtac cagcccaag ccttgacaac ttccataggg tgtcaagcct gtgggtgcac 60
agaagtcaaa aattgagttt tgggatcctc agcctagatt tcagaggata taaagaaaca 120
cctaacacct agatattcag acaaaagttt actacaggga tgaagctttc acggaaaacc 180

tctactagga aagtacagaa gagaaatgtg ggtttggagc ccccaaacag aatcccctct 240
agaacactgc ctaatgaaac tgtgagaaga tggccactgt catccagaca ccagaatgat 300
agacccacca aaaacttatg ccatattgcc tataaaacct acagacactc aatgccagcc 360
ccatgaaaaa aaaactgaga agaagactgt nccctacaat gccaccggag cagaactgcc 420
ccaggccatg gaagcacagc tcttatatca atgtgacctg gatgttgaga catggaatcc 480
nangaaatcn ttttaanact tccacggttn aatgactgcc ctattanatt cngaacttan 540
atccnggcct gtgacctctt tgctttggcc attccccctt tttggaatgg ctnttttttt 600
cccatgcctg tnccctctta 620

<210> 30
<211> 100
<212> DNA
<213> Homo sapien

<400> 30
ttacaacgag ggggtcaatg tcataaatgt cacaataaaa caatctcttc tttttttttt 60
ttttttttct ttttttttct ttttttttct ttttttttct 100

<210> 31
<211> 762
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(762)
<223> n = A,T,C or G

<400> 31
tagtctatgc gccggacaga gcagaattaa attggaagtt gccctccgga ctttctaccc 60
acactcttcc tgaaaagaga aagaaaaaga gcaggaaaga ggttaggatt tcattttcaa 120
gagtcagcta attaggagag cagagtttag acagcagtag gcacccccatg atacaaacca 180
tggacaaagt ccctgtttag taactgccag acatgatcct gctcaggttt tgaaatctct 240
ctgcccataa aagatggaga gcaggagtgc catccacatc aacacgtgtc caagaaagag 300
tctcagggag acaagggtat caaaaaacaa gattcttaat gggaaggaaa tcaaaccaaa 360
aaattagatt tttctctaca tatatataat atacagatat ttaacacatt attccagagg 420
tggctccagt ccttggggct tgagagatgg tgaaaacttt tgttccacat taacttctgc 480
tctcaaattc tgaagtatat cagaatggga caggcaatgt tttgctccac actggggcac 540
agacccaaat ggttctgtgc ccgaagaaga gaagcccgaa agacatgaag gatgcttaag 600
gggggttggg aaagccaaat tggtantatc ttttcctcct gcctgtgttc cngaagtctc 660
cnctgaagga attcttaaaa ccctttgtga ggaaatgccc ccttaccatg acaantggtc 720
ccattgcttt tagggngatg gaaacaccaa gggttttgat cc 762

<210> 32
<211> 276
<212> DNA
<213> Homo sapien

<400> 32
tagtctatgc gtgtattaac ctccccctccc tcagtaacaa ccaaagaggc aggagctgtt 60
attaccaacc ccattttaca gatgcatcaa taatgacaga gaagtgaagt gacttgcgca 120
cacaaccagt aaattggcag agtcagattt gaatccatgg agtctggtct gcactttcaa 180
tcaccgaata ccctttctaa gaaacgtgtg ctgaatgagt gcatggataa atcagtgtct 240
actcaacatc tttgcctaga tatcccgcat agacta 276

<210> 33
<211> 477
<212> DNA
<213> Homo sapien

<400> 33
tagtagttgc caaatatttg aaaatttacc cagaagtgat tgaaaacttt ttggaaacaa 60
aaacaaataa agccaaaagg taaaataaaa atatctttgc actctcgtta ttacctatcc 120
ataacttttt caccgtaagc tctcctgctt gttagtgtag tgtggttata ttaaactttt 180
tagttattat tttttattca cttttccact agaaagtcat tattgattta gcacacatgt 240
tgatctcatt tcatttttte ttttttatagg caaaatttga tgctatgcaa caaaaatact 300
caagcccatt atctttttte cccccgaaat ctgaaaattg caggggacag agggaagtta 360
tcccattaaa aaattgtaaa tatgttcagt ttatgtttaa aaatgcacaa aacataagaa 420
aattgtgttt acttgagctg ctgattgtaa gcagttttat ctcaggggca actacta 477

<210> 34
<211> 631
<212> DNA
<213> Homo sapien

<400> 34
tagtagttgc caattcagat gatcagaaat gctgctttcc tcagcattgt cttgttaaac 60
cgcatgccat ttggaacttt ggcagtgaga agccaaaagg aagaggtgaa tgacatatat 120
atatatatat attcaatgaa agtaaaatgt atatgctcat atactttcta gttatcagaa 180
tgagttaagc tttatgccat tgggctgctg catattttaa tcagaagata aaagaaaatc 240
tgggcatttt tagaatgtga tacatgtttt tttaaaactg ttaaatatta tttcgatatt 300
tgtctaagaa ccggaatgtt cttaaaattt actaaaacag tattgtttga ggaagagaaa 360
actgtactgt ttgccattat tacagtcgta caagtgcatg tcaagtcacc cactctctca 420
ggcatcagta tccacctcat agctttacac attttgacgg ggaatattgc agcatcctca 480
ggcctgacat ctgggaaagg ctcagatcca cctactgctc cttgctcgtt gatttgtttt 540
aaaatattgt gcctggtgtc acttttaagc cacagcctg cctaaaagcc agcagagaac 600
agaacccgca ccattctata ggcaactact a 631

<210> 35
<211> 578
<212> DNA
<213> Homo sapien

<400> 35
tagtagttgc catcccatat tacagaaggc tctgtataca tgacttattt ggaagtgatc 60
tgttttctct ccaaacccat ttatcgtaat ttcaccagtc ttggatcaat cttggtttcc 120
actgatacca tgaaacctac ttggagcaga cattgcacag ttttctgtgg taaaaactaa 180
aggtttattt gctaagctgt catcttatgc ttagtatttt ttttttacag tggggaattg 240
ctgagattac attttgttat tcattagata ctttgggata acttgacact gtcttctttt 300
tttcgctttt aattgctatc atcatgcttt tgaaacaaga acacattagt cctcaagtat 360
tacataagct tgcttgttac gcctggtggt ttaaaggact atctttggcc tcaggttcac 420
aagaatgggc aaagtgtttc cttatgttct gtagttctca ataaaagatt gccaggggcc 480
gggtactgtg gctcgcactg taatcccagc actttgggaa gctgaggctg gcggatcatg 540
ttagggcagg tgttcgaaac cagcctgggc aactacta 578

<210> 36
<211> 583
<212> DNA
<213> Homo sapien

<400> 36
tagtagttgc ctgtaatccc agcaactcag gaggctgggg caggagaatc agttgaacct 60
gggaggcaga agttgtaatt agcaaagatc gcaccattgc acttcagcct gggcaacaag 120
agtgagattc catctcaaaa acaaaaaaaa gaaaaagaaa agaaaaggaa aaaacgtata 180
aacccagcca aaacaaaatg atcattcttt taataagcaa gactaattta atgtgtttat 240
ttaatcaaag cagttgaatc ttctgagtta ttggtgaaaa tacccatgta gttaatttag 300
ggttcttact tgggtgaacg tttgatgttc acaggttata aaatggttaa caaggaaaat 360
gatgcataaa gaatcttata aactactaaa aataaataaa atataaatgg ataggtgcta 420
tggatggagt ttttgtgtaa tttaaaatct tgaagtcatt ttggatgctc attggttgtc 480
tggtaatttc cattaggaaa aggttatgat atggggaaac tgtttctgga aattgcggaa 540
tgtttctcat ctgtaaaatg ctagtatctc agggcaacta cta 583

<210> 37
<211> 716
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(716)
<223> n = A,T,C or G

<400> 37
gatctactag tcatntggat tctatccatg gcagctaagc ctttctgaat ggattctact 60
gctttcttgt tctttaatcc agacccttat atatgtttat gttcacaggc agggcaatgt 120
ttagtgaaaa caattctaaa ttttttattt tgcattttca tgctaatttc cgtcacactc 180
cagcaggctt cctgggagaa taaggagaaa tacagctaaa gacattgtcc ctgcttactt 240
acagcctaat ggtatgcaaa accacttcaa taaagtaaca ggaaaagtac taaccaggta 300
gaatggacca aaactgatat agaaaaatca gaggaagaga ggaacaaata tttactgagt 360
cctagaatgt acaaggcttt ttaattacat attttatgta aggcctgcaa aaaacaggtg 420
agtaatcaac atttgtccca ttttacatat aaggaaactg aagcttaaat tgaataattt 480
aatgcataga ttttatagtt agaccatgtt caggtcccta tgttatactt actagctgta 540
tgaatatgag aaaataattt tgttattttc ttggcatcag tattttcatc tgcaaaataa 600
agctaaagtt atttagcaaa cagtcagcat agtgcctgat acatagtagg tgctccaaac 660
atgattacnc tantattngg tattanaaaa atccaatata ggcntggata aaaccg 716

<210> 38
<211> 688
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(688)
<223> n = A,T,C or G

<400> 38
ttctgtccac atatcatccc actttaattg ttaatcagca aaacttcaa tgaaaaatca 60
tccattttaa ccaggatcac accaggaaac tgaaggtgta ttttttttta ccttaaaaaa 120
aaaaaaaaaa accaaacaaa ccaaaacaga ttaacagcaa agagttctaa aaaatttaca 180
tttctcttac aactgtcatt cagagaacaa tagttcttaa gtctgttaaa tcttggcatt 240
aacagagaaa cttgatgaan agttgtactt ggaatattgt ggatttttt ttttgtctaa 300
tctcccccta ttgttttgcc aacagtaatt taagtttgtg tggaacatcc ccgtagttga 360
agtgtaaaca atgtatagga aggaatatat gataagatga tgcatcacat atgcattaca 420
tgtagggacc ttcacaactt catgcactca gaaaacatgc ttgaagagga ggagaggacg 480

gcccagggtc accatccagg tgccttgagg acagagaatg cagaagtggc actgttgaaa 540
tttagaagac catgtgtgaa tggtttcagg cctgggatgt ttgccaccaa gaagtgcctc 600
cgagaaattt ctttcccatt tggaatacag ggtggcttga tgggtacggt gggtgaccca 660
acgaagaaaa tgaaattctg ccctttcc 688

<210> 39
<211> 585
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(585)
<223> n = A,T,C or G

<400> 39
tagtagttgc cgcnnaccta aaanttggaa agcatgatgt ctaggaaaca tantaaaata 60
gggtatgcct atgtgctaca gagagatgtt agcatttaaa gtgcatantt ttatgtattt 120
tgacaaatgc atatncctct ataatccaca actgattacg aagctattac aattaaaaag 180
tttggccggg cgtggtgggc ggtggctgac gcctgtaatc ccagcacttt gggaggccga 240
ggcacgcgga tcacgaggtc gggagttcaa gaccatcctg gctaacacgg tgaaagtcca 300
tctctactaa aaatacgaaa aaattacccc ggcgtggtgg cgggcgcctg tagtcccagc 360
tactccggag gctgaggcag gagaatggcg tgaacccagg acacggagct tgcagtgtgc 420
caacatcacg tcactgccct ccagcctggg ggacaggaac aagantcccg tcctcanaaa 480
agaaaaatac tactnatant ttcnacttta tttaantta cacagaactn cctcttggta 540
ccccccttacc attcatctca cccacctccc atagggcacn nctaa 585

<210> 40
<211> 475
<212> DNA
<213> Homo sapien

<400> 40
tctgtccaca ccaatcttag aagctctgaa aagaatttgt ctttaaatat cttttaatag 60
taacatgtat tttatggacc aaattgacat tttcgactgt tttttccaaa aaagtcaggt 120
gaatttcagc acactgagtt gggaatttct tatcccagaa gaccaaccaa tttcatattt 180
atttaagatt gattccatac tccgttttca aggagaatcc ctgcagtctc cttaaaggta 240
gaacaaatac ttcctatttt tttttcacca ttgtgggatt ggactttaag aggtgactct 300
aaaaaaacag agaacaaata tgtctcagtt gtattaagca cggacccata ttatcatatt 360
cacttaaaaa aatgatttcc tgtgcacctt ttggcaactt ctcttttcaa tgtagggaaa 420
aacttagtca ccctgaaaac ccacaaaata aataaaactt gtagatgtgg acaga 475

<210> 41
<211> 423
<212> DNA
<213> Homo sapien

<400> 41
taagagggta catcgggtaa gaacgtaggc acatctagag cttagagaag tctggggtag 60
gaaaaaaatc taagtattta taagggtata ggtaacattt aaaagtaggg ctagctgaca 120
ttatttagaa agaacacata cggagagata agggcaaagg actaagacca gaggaacact 180
aatatttagt gatcacttcc attcttggta aaaatagtaa cttttaagtt agcttcaagg 240
aagatttttg gccatgatta gttgtcaaaa gttagttctc ttgggtttat attactaatt 300
ttgttttaag atccttgtta gtgctttaat aaagtcatgt tatatcaaac gctctaaaac 360
attgtagcat gttaaaatgtc acaatatact taccatttgt tgtatatggc tgtacccttct 420

cta 423

<210> 42
<211> 527
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(527)
<223> n = A,T,C or G

<400> 42
tctcctaggc taatgtgtgt gtttctgtaa aagtaaaaag ttaaaaattt taaaaataga 60
aaaaagctta tagaataaga atatgaagaa agaaaatatt tttgtacatt tgcacaatga 120
gtttatgttt taagctaagt gttattacaa aagagccaaa aaggttttaa aaattaaaac 180
gtttgtaaag ttacagtacc cttatgttaa tttataattg aagaaagaaa aacttttttt 240
tataaatgta gtgtagccta agcatacagt atttataaag tctggcagtg ttcaataatg 300
tcctaggcct tcacattcac tcactgactc acccagagca acttccagtc ctgtaagctc 360
cattcgtggt aagtgccctn tacaggtgca ccatttattt tacagtattt ttactgtacc 420
ttctctatgt ttccatatct ttcgatatac aaataccact ggttactatn gcccnacagg 480
taattccagt aacacgggcc gtatacgtct ggtancccta gngaaga 527

<210> 43
<211> 331
<212> DNA
<213> Homo sapien

<400> 43
tcttcaacct cgtaggacaa ctctcatatg cctgggcact atttttaggt tactaccttg 60
gctgcccttc tttaagaaaa aaaaaagaag aaaaaagaac ttttccacaa gtttctcttc 120
ctctagttgg aaaattagag aaatcatgtt tttaattttg tgttatttca gatcacaaat 180
tcaaacactt gtaaacatta agcttctgtt caatcccctg ggaagaggat tcattctgat 240
atttacggtt caaaagaagt tgtaatattg tgcttggaac acagagaacn agttattaac 300
ttcctactac tattatataa taaataataa c 331

<210> 44
<211> 592
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(592)
<223> n = A,T,C or G

<400> 44
ggcttagtag ttgccaggca aaatarcgtt gattctcctc aggagccacc cccaacaccc 60
ctgtttgctt ctagacctat acctagacta aagtcccagc agacccctag aggtgaggtt 120
cagagtgacc cttgaggaga tgtgctacac tagaaaagaa ctgcttgagt tttctaattt 180
atataagcag aaatctggag aagagtcata ggaatggata ttaagggtgt gagataatgg 240
cggaaggaat atagagttgg atcaggctgg acttattgat ttgaacccac taagtagaga 300
ttctgctttt gatgttgcag ctcagggagt taaaaaaggt tttaatggtt ctaatagttt 360
atttgcttgg ttagctgaaa tatggataaa agatggccca ctgtgagcaa gctggaaatg 420
cctgatctct ctcagtttaa tgtagaggaa gggatccaaa agtttaggga ganttggatg 480

ctggraktgg attggtcact ttgrgaccta cccwtcccag ctgggagggt ccagaagata 540
caccettgac caacgctttg cgaaatggat ttgtgatggc ggcaactact aa 592

<210> 45
<211> 567
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(567)
<223> n = A,T,C or G

<400> 45
ggcttagtag ttgccattgc gagtgcttgc tcaacgagcg ttgaacatgg cggattgtct 60
agattcaacg gatttgagtt ttaccagcaa agcgaaccaa gcgcggccca gagaattatg 120
ggttggttgg ctttgaaaag atggaaatcc tgtaggccta gtcagaaaag ccttcttgca 180
gaacagttgg ttctcgggcg aacgctcatc aagatgccca ttggaaaggc tagcgtgtat 240
ttgggagagc ctgatagcgt gtcttctgat gatgtttgtg cttggacagt gacaaaagat 300
atgcaaagca agtccgaact agacgtcaag cttcgtgagc aaattattgt agactcctac 360
ttatactgtg aggaatgata gccaagggtg gggactttaa gactaaggtg gtttgtactt 420
gcgccgatga tcccaggcag aaagamcttg tcgctagttt tatacgggca actactaagc 480
cgaattccag cacactggcg gccgttacta attggatccg anctcggtac cagcttgatg 540
catascttga gttwtctata ntgtcnc 567

<210> 46
<211> 908
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(908)
<223> n = A,T,C or G

<400> 46
gagcgaaaga ccgagggcag ngnntangng cgangaagcg gagagggcca aaaagcaacc 60
gctttccccg gggggtgccg attcattaag gcaggtggag gacaggtttc ccgatggaag 120
gcggcagggg cgcaagcaat taatgtgagt aggccattca ttagcacccg ggcttaacat 180
ttaagcttcg ggttggtatg tggtgggaat tgtgagcgga taacaatttc acacaggaaa 240
cagctatgac catgattacg ccaagctatt taggtgacat tatagaataa ctcaagttat 300
gcatcaagct tggtaccgag ttcggatcca ctagtaacgg ccgccagtgt gtggaattcg 360
gcttagtagt tgccgaccat ggagtgctac ctaggctaga atacctgagy tcctccctag 420
cctcactcac attaaattgt atcttttcta cattagatgt cctcagcgcc ttatttctgc 480
tggacwatcg ataaattaat cctgatagga tgatagcagc agatttaatta ctgagagtat 540
gttaatgtgt catccctcct atataacgta tttgcatttt aatggagcaa ttctggagat 600
aatccctgaa ggcaaaggaa tgaatcttga gggtgagaaa gccagaatca gtgtccagct 660
gcagttgtgg gagaaggtga tattatgtat gtctcagaag tgacaccata tgggcaacta 720
ctaagcccga attccagcac actggcgggc gttactaatg gatccgagct cggtaccaag 780
cttgatgcat agcttgagta tctatagtgt cacctaaatag cctggcgtta tcatggtcat 840
agctgtttcc tgtgtgaaat tgttatccgc tcccaattcc ccccaccata cgagccggaa 900
cataaagt 908

<210> 47
<211> 480

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(480)
<223> n = A,T,C or G

<400> 47
tgccaacaag gaaagtttta aatttcccct tgaggattct tggtgatcat caaattcagt 60
ggtttttaag gttgttttct gtcaaataac tctaacttta agccaaacag tatatggaag 120
cacagataka atattacaca gataaaagag gagttgatct aaagtaraga tagttggggg 180
ctttaatttc tggaacctag gtctccccat cttcttctgt gctgaggaac ttcttggaag 240
cggggattct aaagttcttt ggaagacagt ttgaaaacca ccatgttgtt ctcagtacct 300
ttatttttaa aaagtaggtg aacattttga gagagaaaag ggcttggttg agatgaagtc 360
ccccccccc ctttttttt ttttagctga aatagatacc ctatgttnaa rgaarggatt 420
attatttacc atgccaytar scacatgctc tttgatgggc nyctccstac cctccttaag 480

<210> 48
<211> 591
<212> DNA
<213> Homo sapien

<400> 48
aagagggtac cgagtggaat ttccgcttca ctagtctggt gtggctagtc ggtttcgtgg 60
tggccaacat tacgaacttc caactcaacc gttcttggac gttcaagcgg gagtaccggc 120
gaggatggtg gcgtgaattc tggcctttct ttgccgtggg atcggtagcc gccatcatcg 180
gtatgtttat caagatcttc tttactaacc cgacctctcc gatttacctg cccgagccgt 240
ggtttaacga ggggaggggg atccagtcac gcgagtactg gtcccagatc ttcgccatcg 300
tcgtgacaat gcctatcaac ttcgtcgtca ataagttgtg gaccttccga acggtgaagc 360
actccgaaaa cgtccggtgg ctgctgtgcg gtgactccca aaatcttgat aacaacaagg 420
taaccgaatc gcgctaagga accccggcat ctcgggtact ctgcatatgc gtacccctta 480
agccgaattc cagcacactg gcggccgtta ctaattggat ccgaactccg taaccaagcc 540
tgatgcgtaa cttgagttat tctatagtgt ccctaaaata acctggcgtt a 591

<210> 49
<211> 454
<212> DNA
<213> Homo sapien

<400> 49
aagagggtac ctgccttgaa atttaaatgt ctaaggaaar tgggagatga ttaagagttg 60
gtgtggcyta gtcacaccaa aatgtattta ttacatcctg ctcctttcta gttgacagga 120
aagaaagctg ctgtggggaa aggagggata aatactgaag ggatttacta aacaaatgtc 180
catcacagag ttttcctttt ttttttttg agacagagtc ttgctctgtc acccaggctg 240
gaatgaagwg gtatgatctc agttgaatgc aacctctacc tcctaggttc aagcgattct 300
catgcctcag cctcctgagc agctgggact ataggcgcat gctaccatgc caggctaatt 360
tttatatttt tattagagac ggggtgttgc catgttggcc aggcaggtct cgaactcctg 420
ggcctcagat gatctgcccc accgtaccct ctta 454

<210> 50
<211> 463
<212> DNA
<213> Homo sapien

<400> 50

aagagggtac caaaaaaaag aaaaaggaaa aaaagaaaaa caacttgtat aaggctttct 60
gctgcataca gctttttttt tttaaataaa tggtgccaac aaatgttttt gcattcacac 120
caattgctgg ttttgaaatc gtactcttca aaggtatttg tgcagatcaa tccaatagtg 180
atgccccgta ggttttgtgg actgcccacg ttgtctacct tctcatgtag gagccattga 240
gagactgttt ggacatgcct gtgttcatgt agccgtgatg tccgggggcc gtgtacatca 300
tgttaccgtg gggtggggtc tgcattggct gctgggcata tggctgggtg cccatcatgc 360
ccatctgcat ctgcataggg tattggggcg tttgatccat atagccatga ttgctgtggt 420
agccactgtt catcattggc tgggacatgc tgttaccctc tta 463

<210> 51
<211> 399
<212> DNA
<213> Homo sapien

<400> 51

cttcaacctc ccaaagtgct gggattacag gactgagcca ccacgctcag cctaagcctc 60
tttttcacta ccctctaagc gatctaccac agtgatgagg ggctaaagag cagtgcaatt 120
tgattacaat aatggaactt agatttatta attaacaatt tttccttagc atgttggttc 180
cataattatt aagagtatgg acttacttag aaatgagctt tcattttaag aatttcatct 240
ttgaccttct ctattagtct gagcagtatg acactatacg tattttattt aactaaccta 300
ccttgagcta ttacttttta aaaggctata tacatgaatg tgtattgtca actgtaaagc 360
cccacagtat ttaattatat catgatgtct ttgaggttg 399

<210> 52
<211> 392
<212> DNA
<213> Homo sapien

<400> 52

cttcaacctc aatcaacctt ggtaattgat aaaatcatca cttaactttc tgatataatg 60
gcaataatta tctgagaaaa aaaagtggtg aaagattaaa cttgcatttc tctcagaatc 120
ttgaaggata tttgaataat tcaaaagcgg aatcagtagt atcagccgaa gaaactcact 180
tagctagaac gttggaccca tggatctaag tccctgccct tccactaacc agctgattgg 240
ttttgtgtaa acctcctaca cgcttgggct tggtcgcctc atttgtcaaa gtaaaggctg 300
aaataggaag ataatgaacc gtgtcttttt ggtctctttt ccatccatta ctctgatttt 360
acaaagaggc ctgtattccc ctggtgaggt tg 392

<210> 53
<211> 179
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(179)
<223> n = A,T,C or G

<400> 53

ttcgggtgat gcctcctcag gctacagtga agactggatt acagaaaggt gccagcgaga 60
tttcagattc ctgtaaacct ctaaagaaaa ggagtcgcgc ctcaactgat gtagaaatga 120
ctagttcagc atacngagac acntctgact ccgattctag aggactgagt gacctgcan 179

<210> 54
<211> 112

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(112)
<223> n = A,T,C or G

<400> 54
ttcgggtgat gcctcctcag gctacatcat natagaagca aagtagaana atcnngtttg 60
ngcattttcc cacanacaaa attcaaatga ntggaagaaa ttggganagt at 112

<210> 55
<211> 225
<212> DNA
<213> Homo sapien

<400> 55
tgagcttccg cttctgacaa ctcaatagat aatcaaagga caactttaac agggattcac 60
aaaggagtat atccaaatgc caataaacat ataaaaagga attcagcttc atcatcatca 120
gaagwatgca aattaaaacc ataatgagaa accactatgt cccactagaa tagataaaat 180
cttaaaagac tggtaaaacc aagtgttggt aaggcaagag gagca 225

<210> 56
<211> 175
<212> DNA
<213> Homo sapien

<400> 56
gctcctcttg ccttaccaac acattctcaa aaacctgtta gagtcctaag cattctcctg 60
ttagtattgg gattttaccc ctgtcctata aagatgttat gtaccaaaaa tgaagtggag 120
ggccataccc tgagggaggg gagggatctc tagtgttgtc agaagcggaa gctca 175

<210> 57
<211> 223
<212> DNA
<213> Homo sapien

<400> 57
agccatttac cacccatgga tgaatggatt ttgtaattct agctgttgta ttttgtgaat 60
ttgttaattt tgttgttttt ctgtgaaaca catacattgg atatgggagg taaaggagtg 120
tcccagttgc tcctggtcac tccctttata gccattactg tcttgtttct tgtaactcag 180
gttaggtttt ggtctctctt gctccactgc aaaaaaaaaa aaa 223

<210> 58
<211> 211
<212> DNA
<213> Homo sapien

<400> 58
gttcgaaggt gaacgtgtag gtagcggatc tcacaactgg ggaactgtca aagacgaatt 60
aactgacttg gatcaatcaa atgtgactga ggaaacacct gaaggtgaag aacatcatcc 120
agtggcagac actgaaaata aggagaatga agttgaagag gtaaaagagg agggtccaaa 180
agagatgact ttggatgggt ggtaaatggc t 211

<210> 59
<211> 208
<212> DNA
<213> Homo sapien

<400> 59
gctcctcttg ccttaccaac tttgcaccca tcatcaacca tgtggccagg tttgcagccc 60
aggctgcaca tcaggggact gcctcgcaat acttcatgct gttgctgctg actgatggtg
120ctgtgacgga tgtggaagcc acacgtgagg ctgtggtgcg tgcctcgaac ctgcccatgt
180
cagtgatcat tatgggtggt aaatggct 208

<210> 60
<211> 171
<212> DNA
<213> Homo sapien

<400> 60
agccatttac cacccatact aaattctagt tcaaactcca acttcttcca taaaacatct 60
aaccactgac accagttggc aatagcttct tccttcttta acctcttaga gtatttatgg 120
tcaatgccac acatttctgc aactgaataa agttggtaag gcaagaggag c 171

<210> 61
<211> 134
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(134)
<223> n = A,T,C or G

<400> 61
cgggtgatgc ctcctcaggc tttggtgtgt ccactcnact cactggcctc ttctccagca 60
actggtgaan atgtcctcan gaaaancncc acacgcngct cagggtgggg tgggaancat 120
canaatcatc nggc 134

<210> 62
<211> 145
<212> DNA
<213> Homo sapien

<400> 62
agagggtaca tatgcaacag tatataaagg aagaagtgca ctgagaggaa cttcatcaag 60
gccatttaat caataagtga tagagtcaag gctcaaccca ggtgtgacgg attccaggtc 120
ccaagctcct tactggtacc ctctt 145

<210> 63
<211> 297
<212> DNA
<213> Homo sapien

<400> 63
tgcactgaga ggaattcaaa gggtttatgc caaagaacaa accagtcctc tgcagcctaa 60
ctcatttgtt tttgggctgc gaagccatgt agagggcgat caggcagtag atggtccctc 120

ccacagtcag cgccatggtg gtccggtaaa gcatttggtc aggcaggcct cgtttcaggt 180
agacgggcac acatcagctt tctggaaaaa cttttgtagc tctggagctt tgtttttccc 240
agcataatca tacactgtgg aatcggaggt cagtttagtt ggtaaggcaa gaggagc 297

<210> 64
<211> 300
<212> DNA
<213> Homo sapien

<400> 64
gcactgagag gaacttccaa tactatgttg aataggagtg gtgagagagg gcatccttgt 60
cttgtgccgg ttttcaaagg gaatgcttcc agcttttgcc cattcagtat aatattaaag 120
aatgttttac cattttctgt cttgcctgtt tttctgtgtt tttgttggtc tcttcattct 180
ccatttttag gcctttacat gttaggaata tatttctttt aatgatactt caccttggt 240
atcttttgtg agactctact catagtgtga taagcactgg gttggtaagg caagaggagc 300

<210> 65
<211> 203
<212> DNA
<213> Homo sapien

<400> 65
gctcctcttg ccttaccaac tcacccagta tgtcagcaat tttatcrgct ttacctacga 60
aacagcctgt atccaaacac ttaacacact cacctgaaaa gttcaggcaa caatcgcctt 120
ctcatgggtc tctctgctcc agttctgaac ctttctcttt tcctagaaca tgcatttarg 180
tcgatagaag ttcctctcag tgc 203

<210> 66
<211> 344
<212> DNA
<213> Homo sapien

<400> 66
tacggggacc cctgcattga gaaagcgaga ctcactctga agctgaaatg ctgttgccct 60
tgcagtgctg gtagcaggag ttctgtgctt tgtgggctaa ggctcctgga tgacccctga 120
catggagaag gcagagttgt gtgccccttc tcatggcctc gtcaaggcat catggactgc 180
cacacacaaa atgccgtttt tattaacgac atgaaattga aggagagaac acaattcact 240
gatgtggctc gtaaccatgg atatggtcac atacagaggt gtgattatgt aaaggttaat 300
tccacccacc tcatgtggaa actagcctca atgcaggggt ccca 344

<210> 67
<211> 157
<212> DNA
<213> Homo sapien

<400> 67
gcactgagag gaacttcgta gggaggttga actggctgct gaggaggggg aacaacaggg 60
taaccagact gatagccatt ggatggataa tatggtggtt gaggagggac actacttata 120
gcagagggtt gtgtatagcc tgaggaggca tcacccg 157

<210> 68
<211> 137
<212> DNA
<213> Homo sapien

<400> 68
gcactgagag gaacttctag aaagtgaaag tctagacata aaataaaata aaaatttaaa 60
actcaggaga gacagcccag cacggtggct cacgcctgta atcccagaac tttgggagcc 120
tgaggaggca tcacccg 137

<210> 69
<211> 137
<212> DNA
<213> Homo sapien

<400> 69
cgggtgatgc ctcctcaggc tgtattttga agactatcga ctggacttct tatcaactga 60
agaatccgtt aaaaatacca gttgtattat ttctacctgt caaaatccat ttcaaatgtt 120
gaagttcctc tcagtgc 137

<210> 70
<211> 220
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(220)
<223> n = A,T,C or G

<400> 70
agcatgttga gcccagacac gcaatctgaa tgagtgtgca cctcaagtaa atgtctacac 60
gctgcctggt ctgacatggc acaccatcnc gtggagggca casctctgct cngcctacwa 120
cgagggcant ctcatwgaca ggttccaccc accaaactgc aagaggctca nnaagtactr 180
ccagggtmya sggacmasgg tgggaytyca ycacwcatct 220

<210> 71
<211> 353
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(353)
<223> n = A,T,C or G

<400> 71
cgttagggtc tctatccact gctaaaccat acacctgggt aaacagggac catttaacat 60
tcccanctaa atatgccaag tgacttcaca tgtttatctt aaagatgtcc aaaacgcaac 120
tgatttttctc ccctaaacct gtgatggtgg gatgattaan cctgagtggt ctacagcaag 180
ttaagtgcaa ggtgctaaat gaangtgacc tgagatacag catctacaag gcagtacctc 240
tcaacncagg gcaactttgc ttctcanagg gcatttagca gtgtctgaag taatttctgt 300
attacaactc acggggcggg gggtgaatat ctantggana gnagacccta acg 353

<210> 72
<211> 343
<212> DNA
<213> Homo sapien

<400> 72

gcactgagag gaacttccaa tacyatkatc agagtgaaca rgcarccyac agaacaggag 60
aaaatgttyg caatctctcc atctgacaaa aggctaatat ccagawtcta awaggaactt 120
aaacaaattt atgagaaaag aacaracaac ctcawcaaaa agtgggtgaa ggawatgcts 180
aaargaagac atytattcag ccagtaaaca yatgaaaaaa aggctcatsa tcactgawca 240
ttagagaaat gcaaatcaaa accacaatga gataccatct yayrccagtt agaayggtga 300
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<223> n = A,T,C or G

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tcaaagttcc catgctgcca aagtgccatc ctttggggta ctgttttctg agctccagtg 180
ataactcatt tatacaaggg agatacccag aaaaaaagtg agcaaatctt aaaaaggtgg 240
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<212> DNA
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tcaaagttcc catgctgcca aagtgccatc ctttggggta ctgttttctg agctccagtg 180
ataactcatt tatacaaggg agatacccag aaaaaaagtg agcaaatctt aaaaaggtgg 240
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<212> DNA
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agtcagataa ccttagcttc ctcatatgca aaatgagaat gaaaagtact catcgctgaa 180
ttgttttgag gattagaaaa acatctggca tgcagtagaa attcaattag tattcatttt 240
cattcttcta aattaaacaa ataggatttt tagtggtgga acttcagaca ccagaaatgg 300
gagtggatag agaccct 317

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<212> DNA
<213> Homo sapien

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ttgccatggt ggtttgctgc acccatcagt ccatcatcta cattaggtat ttctcctaat 180
gctatccctc ccctagcccc ttacaccccc aacaggctct agtgtgtgaa gttcctctca 240
gtgc 244

<210> 77
<211> 254
<212> DNA
<213> Homo sapien

<400> 77

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gataataaag gttaatatta ataatgattt attttaaggc attcccraat ttgcataatt 180
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cctgagggga cgcaggaccc ttatgaccct cagaatcttc acaacgggag atggcactgg 180
attgantccc antgacacca gagacacccc aaccaccagn atatcantat attgatgtag 240
ttcctgtaga nggccccctt gtggaggaaa gctccatnag ttggtcatct tcaacaggat 300
ctcaacagtt tccgatggct gtgatgggca tagtcatant taaccntgtn tcgaa 355

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<212> DNA
<213> Homo sapien

<400> 79

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ccccagtgac agctaggatg tgcattctcc agccatcaag agactgagtc aagttgttcc 180
ttaagtcaga acagcagact cagctctgac attctgattc gaatgacact gttcaggaat 240
cggaatcctg tcgattagac tggacagctt gtggcaagtg aatttgcctg taacaagcca 300
gatttttaa aatttatatt gtaaataatg tgtgtgtgtg tgtgtgtata tatatatata 360
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<211> 327
<212> DNA

<213> Homo sapien

<400> 80

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tgtagggctc atggtagggg taaaaggagg gcaatttcta gatcaaataa taagaaggta 180
atagctacta agaagaattt tatggagaaa gggacgcggg cgggggatat agggtcgaag 240
ccgcactcgt aaggggtgga ttttttctatg tagccgttga gttgtggtag tcaaaatgta 300
ataattatta gtagtaagcc taggaga 327

<210> 81
<211> 318
<212> DNA
<213> Homo sapien

<400> 81

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catgcttttt atgttttgtc tgacataaac tcttatcaga gccctttgca cacagggatt 180
caataaatat taacacagtc tacatttatt tggtgaatat tgcatatctg ctgtactgaa 240
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atgattgcgc atagacta 318

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<211> 338
<212> DNA
<213> Homo sapien

<400> 82

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ctgatcaaat atcactctcc tacttacagg actcaacata ctagtcacag ccctatactc 180
cctctacata tttaccacaa cacaatgggg ctcactcacc caccacatta acaacataaa 240
accctcattc acacgagaaa acaccctcat gttcatacac ctatccccca ttctcctcct 300
atccctcaac cccgacatca ttaccgggtt ttcctctt 338

<210> 83
<211> 111
<212> DNA
<213> Homo sapien

<400> 83

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atagactttg aacaaaaagg aacatttgct ggcctgagga ggcatcaccc g 111

<210> 84
<211> 224
<212> DNA
<213> Homo sapien

<400> 84

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tgaggtggat tcacgagttg cggacaactc ctttgatgcc aagcgaggtg cagccggaga 180
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<212> DNA
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<400> 85
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gagcagactt gtaacactct twttgtggaa tttgcaagtg gagatttcag scgctttgaa 180
gtsaaaggta gaaaaggaaa tatcttccta taaaaactag acagaatgat tctcagaaac 240
tcctttgtga tgtgtgcgtt caactcacag agtttaacct ttcwtttcat agaagcagtt 300
aggaaacact ctgtttgtaa agtctgcaag tggatagaga ccctaacg 348

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tttgwggycw wysktmgaaw mggrwatatc ttcwyatmra amctagacag aaksattctc 180
akaawstyyy ytgtgawgws tgcrttcaac tcacagagkt kaacmwtyct kytsatrgag 240
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<210> 88
<211> 10
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<400> 88
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<210> 89
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<210> 91
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<210> 92
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<210> 93
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<210> 95
<211> 10
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<210> 101
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<220>
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<210> 102
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<210> 103
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<210> 104
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<212> DNA
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<220>
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<400> 104
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<210> 105
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<220>
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<400> 105
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<210> 106
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<220>
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<400> 107
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<210> 108
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<210> 112
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<210> 127
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<400> 127
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<210> 128
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<400> 128
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<210> 129
<211> 24
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<210> 130
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<220>
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<400> 130
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<210> 131
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Predicited Th Motifs (B-cell epitopes)

<400> 131
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Gly Ile

<210> 132
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> Predicited Th Motifs (B-cell epitopes)

<221> VARIANT
<222> (1)...(22)
<223> Xaa = Any Amino Acid

<400> 132
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1 5 10 15
Val Gln Gly His Asp Glu
20

<210> 133
<211> 23
<212> PRT
<213> Artificial Sequence

<220>
<223> Predicited Th Motifs (B-cell epitopes)

<400> 133
Ser Pro Gly Val Phe Leu Glu His Leu Gln Glu Ala Tyr Arg Ile Tyr
1 5 10 15
Thr Pro Phe Asp Leu Ser Ala
20

<210> 134
<211> 9
<212> PRT
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<220>
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<210> 135
<211> 9
<212> PRT
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<220>
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<210> 136
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<220>
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<221> VARIANT
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1 5

<210> 137
<211> 9
<212> PRT
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<220>
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Glu Val Val Gln Gly His Asp Glu Ser
1 5

<210> 138
<211> 9
<212> PRT
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<220>
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His Leu Gln Glu Ala Tyr Arg Ile Tyr
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<210> 139
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Predicited HLA A2.1 Motifs (T-cell epitopes)

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1 5

<210> 140
<211> 9
<212> PRT
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<220>
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1 5

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<211> 9388
<212> DNA
<213> Homo sapien

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gctgaggagg attagtaaaa gaggaaggcc tctttgcagt tgaggtaaga ggaaggcatc 540
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ttatgttatg tttataataa agcacccccaa cctttacaaa atctcacttt ttgccagttg   1920
tattatttag tggactgtct ctgataagga cagccagtta aaatggaatt ttgttgttgc   1980
taattaaacc aatttttagt tttggtgttt gtcctaatag caacaacttc tcaggctttа   2040
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ttttaaagga agtaagttcc tggttttgat atcttagtag tgtaatgccc aacctggttt   2160
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<211> 419
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<213> Homo sapien

<400> 142
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<210> 143
<211> 402
<212> DNA

<213> Homo sapien

<400> 143

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<211> 224
<212> DNA
<213> Homo sapien

<400> 144

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<210> 145
<211> 111
<212> DNA
<213> Homo sapien

<400> 145

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<210> 146
<211> 585
<212> DNA
<213> Homo sapien

<400> 146

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<211> 579
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature

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<223> n = A,T,C or G

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<211> 249
<212> DNA
<213> Homo sapien

<400> 148
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<210> 149
<211> 255
<212> DNA
<213> Homo sapien

<400> 149
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<210> 150
<211> 318
<212> DNA
<213> Homo sapien

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<210> 151
<211> 323
<212> DNA

<213> Homo sapien

<220>
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<222> (1)...(323)
<223> n = A,T,C or G

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<210> 152
<211> 311
<212> DNA
<213> Homo sapien

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<211> 332
<212> DNA
<213> Homo sapien

<400> 153
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<210> 154
<211> 345
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
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<223> n = A,T,C or G

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<210> 155
<211> 295
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(295)
<223> n = A,T,C or G

<400> 155
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<210> 156
<211> 406
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(406)
<223> n = A,T,C or G

<400> 156
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<210> 157
<211> 208
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(208)
<223> n = A,T,C or G

<400> 157
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<210> 158
<211> 547
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(547)
<223> n = A,T,C or G

<400> 158
cttcaacctc cttcaacctc cttcaacctc ctggattcaa acaatcatcc cacctcagac 60
tccttagtag ctgagactac agactcacgc cactacatct ggctaaattt ttgtagagat 120
agggtttcat catgttgccc tggctggtct caaactcctg acctcaagca atgtgcccac 180
ctcagcctcc caaagtgctg ggattacagg cataagccac catgcccagt ccatntttaa 240
tctttcctac cacattctta ccacactttc ttttatgttt agatacataa atgcttacca 300
ttatgataca attgcccaca gtattaagac agtaacatgc tgcacaggtt tgtagcctag 360
gaacagtagg caataccaca tagcttaggt gtgtggtaga ctataccatc taggtttgtg 420
taagttacac tttatgctgt ttacacaatg acaaaaccat ctaatgatgc atttctcaga 480
atgtatcctt gtcagtaagc tatgatgtac agggaacact gcccaaggac acagatattg 540
tacctgt 547

<210> 159
<211> 203
<212> DNA
<213> Homo sapien

<400> 159
gctcctcttg ccttaccaac tcacccagta tgtcagcaat tttatcrgct ttacctacga 60
aacagcctgt atccaaacac ttaacacact cacctgaaaa gttcaggcaa caatcgcctt 120
ctcatgggtc tctctgctcc agttctgaac ctttctcttt tcctagaaca tgcatttarg 180
tcgatagaag ttcctctcag tgc 203

<210> 160
<211> 402
<212> DNA
<213> Homo sapien

<400> 160
tgtaagtcga gcagtgtgat gggtggaaca gggttgtaag cagtaattgc aaactgtatt 60
taaacaataa taataatatt tagcatttat agagcacttt atatcttcaa agtacttgca 120
aacattayct aattaaatac cctctctgat tataatctgg atacaaatgc acttaaactc 180
aggacagggt catgagaraa gtatgcattt gaaagttggt gctagctatg ctttaaaaac 240
ctatacaatg atgggraagt tagagttcag attctgttgg actgtttttg tgcatttcag 300
ttcagcctga tggcagaatt agatcatatc tgcactcgat gactytgctt gataacttat 360
cactgaaatc tgagtgttga tcatcacact gctcgactta ca 402

<210> 161
<211> 193
<212> DNA
<213> Homo sapien

<400> 161
agcatgttga gcccagacac tgaccaggag aaaaaccaac caatagaaac acgcccagac 60

actgaccagg agaaaaacca accaataaaa acaggcccgg acataagaca aataataaaa 120
ttagcggaca aggacatgaa aacagctatt gtaagagcgg atatagtggt gtgtgtctgg 180
gctcaacatg cta 193

<210> 162
<211> 147
<212> DNA
<213> Homo sapien

<400> 162
tgttgagccc agacactgac caggagaaaa accaaccaat aaaaacaggc ccggacataa 60
gacaaataat aaaattagcg gacaaggaca tgaaaacagc tattgtaaga gcggatatag 120
tggtgtgtgt ctgggctcaa catgcta 147

<210> 163
<211> 294
<212> DNA
<213> Homo sapien

<400> 163
tagcatgttg agcccagaca caaatctttc cttaagcaat aaatcatttc tgcatatgtt 60
tttaaaacca cagctaagcc atgattattc aaaaggacta ttgtattggg tattttgatt 120
tgggttctta tctccctcac attatcttca tttctatcat tgacctctta tcccagagac 180
tctcaaactt ttatgttata caaatcacat tctgtctcaa aaaatatctc acccacttct 240
cttctgtttc tgcgtgtgta tgtgtgtgtg tgtgtgtctg ggctcaacat gcta 294

<210> 164
<211> 412
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(412)
<223> n = A,T,C or G

<400> 164
cgggattggc tttgagctgc agatgctgcc tgtgaccgca cccggcgtgg aacagaaagc 60
cacctggctg caagtgcgcc agagccgccc tgactacgtg ctgctgtggg gctggggcgt 120
gatgaactcc accgccctga aggaagccca ggccaccgga taccccgcg acaagatgta 180
cggcgtgtgg tgggccggtg cggagcccga tgtgcgtgac gtgggcgaag gcgccaaggg 240
ctacaacgcg ctggctctga acggctacgg cacgcagtcc aaggtgatcc angacatcct 300
gaaacacgtg cacgacaagg gccagggcac ggggcccaaa gacgaagtgg gctcggtgct 360
gtacacccgc ggcgtgatca tccagatgct ggacaaggtg tcaatcacta at 412

<210> 165
<211> 361
<212> DNA
<213> Homo sapien

<400> 165
ttgacacctt gtccagcatc tgcatctgat gagagcctca gatggctacc actaatggca 60
gaaggcaaag gagaacaggc attgtatggc aagaaaggaa gaaagagaga ggggagaaag 120
gtgctaggtt cttttcaaca accagttctt gatggaactg agagtaagag ctcaaggcca 180
ggtgtggtga ctccaaccag taatcccaac attttaggag gctgaggcag gcagatgtct 240

tgaccccatg agtttgtgac cagcctgaac aacatcatga gactccatct ctacaataat 300
tacaaaaatt aatcaggcat tgtggtatgc cctgtagtcc cagatgctgg acaaggtgtc 360
a 361

<210> 166
<211> 427
<212> DNA
<213> Homo sapien

<400> 166
twgactgact catgtcccct acacccaact atcttctcca ggtggccagg catgatagaa 60
tctgatcctg acttagggga atattttctt tttacttccc atcttgattc cctgccggtg 120
agtttcctgg ttcagggtaa gaaaggagct caggccaaag taatgaacaa atccatcctc 180
acagacgtac agaataagag aacwtggacw tagccagcag aacmcaaktg aaamcagaac 240
mcttamctag gatracaame mcrraratar ktgcycmcmc wtataataga aaccaaactt 300
gtatctaatt aaatatttat ccacygtcag ggcattagtg gttttgataa atacgctttg 360
gctaggattc ctgaggttag aatggaaraa caattgcamc gagggtaggg gacatgagtc 420
aktctaa 427

<210> 167
<211> 500
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(500)
<223> n = A,T,C or G

<400> 167
aacgtcgcat gctcccggcc gccatggccg cgggatagac tgactcatgt cccctaagat 60
agaggagaca cctgctaggt gtaaggagaa gatggttagg tctacggagg ctccagggtg 120
ggagtagttc cctgctaagg gagggtagac tgttcaacct gttcctgctc cggcctccac 180
tatagcagat gcgagcagga gtaggagaga gggaggtaag agtcagaagc ttatgttgtt 240
tatgcgggga aacgccrtat cgggggcagc cragttatta ggggacantr tagwyartcw 300
agntagcatc caaagcgngg gagttntccc atatggttgg acctgcaggc ggccgcatta 360
gtgattagca tgtgagcccc agacacgcat agcaacaagg acctaaactc agatcctgtg 420
ctgattactt aacatgaatt attgtatttt tttaacaact ttgagttatg aggcatatta 480
ttaggtccat attacctgga 500

<210> 168
<211> 358
<212> DNA
<213> Homo sapien

<400> 168
ttcatcgctc ggtgactcaa gcctgtaatc ccagaacttt gggaggccga ggggagcaga 60
tcacctgagg ttgggagttt gagaccagcc tggccaacat ggtgacaacc cgtctctgct 120
aaaaatacaa aaattagcca agcatggtgg catgcacttg taatcccagc tactcgggag 180
gctgaggcag gagaatcact tgaggccagg aggcagaggt tgcagtgagg cagaggttga 240
gatcatgcca ctgcactcca gcctgggcaa cagagtaaga ctccatctca aaaaaaaaaa 300
aaaaaaagaa tgatcagagc cacaaataca gaaaaccttg agtcaccgag cgatgaaa 358

<210> 169
<211> 1265

<212> DNA
<213> Homo sapien

<400> 169
ttctgtccac accaatctta gagctctgaa agaatttgtc tttaaatatc ttttaatagt 60
aacatgtatt ttatggacca aattgacatt ttcgactatt ttttcccaaa aaaagtcagg 120
tgaatttcag cacactgagt tgggaatttc ttatcccaga agwcggcacg agcaatttca 180
tatttattta agattgattc catactccgt tttcaaggag aatccctgca gtctccttaa 240
aggtagaaca aatactttct attttttttt caccattgtg ggattggact ttaagaggtg 300
actctaaaaa aacagagaac aaatatgtct cagttgtatt aagcacggac ccatatttatc 360
atattcactt aaaaaaatga tttcctgtgc acctttttggc aacttctctt ttcaatgtag 420
ggaaaaactt agtcaccctg aaaacccaca aaataaataa aacttgtaga tgtgggcaga 480
argtttgggg gtggacattg tatgtgttta aattaaaccc tgtatcactg agaagctgtt 540
gtatgggtca gagaaaatga atgcttagaa gctgttcaca tcttcaagag cagaagcaaa 600
ccacatgtct cagctatatt attatttatt ttttatgcat aaagtgaatc atttcttctg 660
tattaatttc caaagggttt taccctctat ttaaatgctt tgaaaaacag tgcattgaca 720
atgggttgat atttttcttt aaaagaaaaa tataattatg aaagccaaga taatctgaag 780
cctgttttat tttaaaactt tttatgttct gtggttgatg ttgtttgttt gtttgtttct 840
attttgttgg ttttttactt tgtttttttgt tttgttttgt tttggtttdg catactacat 900
gcagtttctt taaccaatgt ctgtttggct aatgtaatta aagttgttaa tttatatgag 960
tgcatttcaa ctatgtcaat ggtttcttaa tatttattgt gtagaagtac tggtaatttt 1020
tttatttaca atatgtttaa agagataaca gtttgatatg ttttcatgtg tttatagcag 1080
aagttattta tttctatggc attccagcgg atattttggt gtttgcgagg catgcagtca 1140
atattttgta cagttagtgg acagtattca gcaacgcctg atagcttctt tggccttatg 1200
ttaaataaaa agacctgttt gggatgtaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1260
aaaaa 1265

<210> 170
<211> 383
<212> DNA
<213> Homo sapien

<400> 170
tgtaagtcga gcagtgtgat gacgatattc ttcttattaa tgtggtaatt gaacaaatga 60
tctgtgatac tgatcctgag ctaggaggcg ctgttcagtt aatgggactt cttcgtactc 120
taattgatcc agagaacatg ctggctacaa ctaataaaac cgaaaaaagt gaatttctaa 180
atttttttcta caaccattgt atgcatgttc tcacagcacc acttttgacc aatacttcag 240
aagacaaatg tgaaaaggat aatatagttg gatcaaacaa aaacaacaca atttgtcccg 300
ataattatca aacagcacag ctacttgcct taattttaga gttactcaca ttttgtgtgg 360
aacatcacac tgctcgactt aca 383

<210> 171
<211> 383
<212> DNA
<213> Homo sapien

<400> 171
tgggcacctt caatatcgca agttaaaaat aatgttgagt ttattatact tttgacctgt 60
ttagctcaac agggtgaagg catgtaaaga atgtggactt ctgaggaatt ttcttttaaa 120
aagaacataa tgaagtaaca ttttaatttac tcaaggacta cttttggttg aagtttataa 180
tctagatacc tctacttttt gtttttgctg ttcgacagtt cacaaagacc ttcagcaatt 240
tacagggtaa aatcgttgaa gtagtggagg tgaaactgaa atttaaaatt attctgtaaa 300
tactataggg aaagaggctg agcttagaat cttttggttg ttcatgtgtt ctgtgctctt 360
atcatcacac tgctcgactt aca 383

<210> 172
<211> 699
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(699)
<223> n = A,T,C or G

<400> 172
tcgggtgatg cctcctcagg cttgtcgtta gtgtacacag agctgctcat gaagcgacag 60
cggctgcccc tggcacttca gaacctcttc ctctacactt ttggtgcgct tctgaatcta 120
ggtctgcatg ctggcggcgg ctctggccca ggcctcctgg aaagtttctc aggatgggca 180
gcactcgtgg tgctgagcca ggcactaaat ggactgctca tgtctgctgt catggagcat 240
ggcagcagca tcacacgcct ctttgtggtg tcctgctcgc tggtggtcaa cgccgtgctc 300
tcagcagtcc tgctacggct gcagctcaca gccgccttct tcctggccac attgctcatt 360
ggcctggcca tgcgcctgta ctatggcagc cgctagtccc tgacaacttc caccctgatt 420
ccggaccctg tagattgggc gccaccacca gatccccctc ccaggccttc ctccctctcc 480
catcagcggc cctgtaacaa gtgccttgtg agaaaagctg gagaagtgag ggcagccagg 540
ttattctctg gaggttggtg gatgaagggg taccctagg agatgtgaag tgtgggtttg 600
gttaaggaaa tgcttaccat cccccacccc caaccaagtt nttccagact aaagaattaa 660
ggtaacatca atacctaggc ctgaggaggc atcacccga 699

<210> 173
<211> 701
<212> DNA
<213> Homo sapien

<400> 173
tcgggtgatg cctcctcagg ccagatcaaa cttggggttg aaaactgtgc aaagaaatca 60
atgtcggaga aagaattttg caaaagaaaa atgcctaatc agtactaatt taataggtca 120
cattagcagt ggaagaagaa atgttgatat tttatgtcag ctattttata atcaccagag 180
tgcttagctt catgtaagcc atctcgtatt cattagaaat aagaacaatt ttattcgtcg 240
gaaagaactt ttcaatttat agcatcttaa ttgctcagga ttttaaattt tgataaagaa 300
agctccactt ttggcaggag taggggcag ggagagagga ggctccatcc acaaggacag 360
agacaccagg gccagtaggg tagctggtgg ctggatcagt cacaacggac tgacttatgc 420
catgagaaga aacaacctcc aaatctcagt tgcttaatac aacacaagct catttcttgc 480
tcacgttaca tgtcctatgt agatcaacag caggtgactc agggacccag gctccatctc 540
catatgagct tccatagtca ccaggacacg ggctctgaaa gtgtcctcca tgcagggaca 600
catgcctctt cctttcattg ggcagagcaa gtcacttatg gccagaagtc acactgcagg 660
gcagtgccat cctgctgtat gcctgaggag gcatcacccg a 701

<210> 174
<211> 700
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(700)
<223> n = A,T,C or G

<400> 174
tcgggtgatg cctcctcang cccctaaatc agagtccagg gtcagagcca caggagacag 60

ggaaagacat agattttaac cggccccctt caggagattc tgaggctcag ttcactttgt 120
tgcagtttga acagaggcag caaggctagt ggttaggggc acggtctcta aagctgcact 180
gcctggatct gcctcccagc tctgccagga accagctgcg tggccttgag ctgctgacac 240
gcagaaagcc ccctgtggac ccagtctcct cgtctgtaag atgaggacag gactctagga 300
acccttccc ttggtttggc ctcactttca caggctccca tcttgaactc tatctactct 360
tttcctgaaa ccttgtaaaa gaaaaaagtg ctagcctggg caacatggca aaaccctgtc 420
tctacaaaaa atacaaaaat tagttgggtg tggtggcatg tgcctgtagt cccagccact 480
tgggaggtgc tgaggtggga ggatcacttg agcccgggag gtggaggttg cagtgagcca 540
agatcatgcc actgcactcc agcctgagta atagagtaag actctgtctc aaaaacaaca 600
acaacaacag tgagtgtgcc tctgtttccg ggttggatgg ggcaccacat ttatgcatct 660
ctcagatttg gacgctgcag cctgaggagg catcacccga 700

<210> 175
<211> 484
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(484)
<223> n = A,T,C or G

<400> 175
tatagggcga attgggcccg agttgcatgn tcccggccgc catggccgcg ggattcgggt 60
gatgcctcct caggcttgtc tgccacaagc tacttctctg agctcagaaa gtgccccttg 120
atgagggaaa atgtcctact gcactgcgaa tttctcagtt ccattttacc tccgagtcct 180
ccttctaaac cagttaataa attcattcca caagtattta ctgattacct gcttgtgcca 240
gggactattc tcaggctgaa gaaggtggga ggggagggcg gaacctgagg agccacctga 300
gccagcttta tatttcaacc atggctggcc catctgagag catctcccca ctctcgccaa 360
cctatcgggg catagcccag ggatgccccc aggcggccca ggttagatgc gtccctttgg 420
cttgtcagtg atgacataca ccttagctgc ttagctggtg ctggcctgag gaggcatcac 480
ccga 484

<210> 176
<211> 432
<212> DNA
<213> Homo sapien

<400> 176
tcgggtgatg cctcctcagg gctcaacgga tgagaagtga cttctttctg gagggaccgt 60
tcatgccacc caggatgaaa atggataggg acccacttgg aggacttgct gatatgtttg 120
gacaaatgcc aggtagcgga attggtactg gtccaggagt tatccaggat agattttcac 180
ccaccatggg acgtcatcgt tcaaatcaac tcttcaatgg ccatggggga cacatcatgc 240
ctcccacaca atcgcagttt ggagagatgg gaggcaagtt tatgaaaagc caggggctaa 300
gccagctcta ccataaccag agtcagggac tcttatccca gctgcaagga cagtcgaagg 360
atatgccacc tcggttttct aagaaaggac agcttaatgc agatgagatt agcctgagga 420
ggcatcaccc ga 432

<210> 177
<211> 788
<212> DNA
<213> Homo sapien

<400> 177
tagcatgttg agcccagaca cagtagcatt tgtgccaatt tctggttgga atggtgacaa 60

catgctggag ccaagtgcta acatgccttg gttcaaggga tggaaagtca cccgtaagga 120
tggcaatgcc agtggaacca cgctgcttga ggctctggac tgcatcctac caccaactcg 180
cccaactgac aagcccttgc gcctgcctct ccaggatgtc tacaaaattg gtggtattgg 240
tactgttcct gttggccgag tggagactgg tgttctcaaa cccggtatgg tggtcacctt 300
tgctccagtc aacgttacaa cggaagtaaa atctgtcgaa atgcaccatg aagctttgag 360
tgaagctctt cctggggaca atgtgggctt caatgtcaag aatgtgtctg tcaaggatgt 420
tcgtcgtggc aacgttgctg gtgacagcaa aaatgaccca ccaatggaag cagctggctt 480
cactgctcag gtgattatcc tgaaccatcc aggccaaata agtgccggct atgcccctgt 540
attggattgc cacacggctc acattgcatg caagtttgct gagctgaagg aaaagattga 600
tcgccgttct ggtaaaaagc tggaagatgg ccctaaattc ttgaagtctg gtgatgctgc 660
cattgttgat atggttcctg gcaagcccat gtgtgttgag agcttctcag actatccacc 720
tttgggtcgc tttgctgttc gtgatatgag acagacagtt gcggtgggtg tctgggctca 780
acatgcta 788

<210> 178
<211> 786
<212> DNA
<213> Homo sapien

<400> 178
tagcatgttg agcccagaca cctgtgtttc tgggagctct ggcagtggcg gattcatagg 60
cacttgggct gcactttgaa tgacacactt ggctttatta gattcactag tttttaaaaa 120
attgttgttc gtttcttttc attaaaggtt taatcagaca gatcagacag cataattttg 180
tatttaatga cagaaacgtt ggtacatttc ttcatgaatg agcttgcatt ctgaagcaag 240
agcctacaaa aggcacttgt tataaatgaa agttctggct ctagaggcca gtactctgga 300
gtttcagagc agccagtgat tgttccagtc agtgatgcct agttatatag aggaggagta 360
cactgtgcac tctttctaggt gtaagcgtat gcaactttgg atcttaaaat tctgtacaca 420
tacacacttt atatatatgt atgtatgtat gaaaacatga aattagtttg tcaaatatgt 480
gtgtgtttag tattttagct tagtgcaact atttccacat tatttattaa attgatctaa 540
gacactttct tgttgacacc ttgaatatta atgttcaagg gtgcaatgtg tattccttta 600
gattgttaaa gcttaattac tatgatttgt agtaaattaa cttttaaaat gtatttgagc 660
ccttctgtag tgtcgtaggg ctcttacagg gtgggaaaga ttttaatttt ccagttgcta 720
attgaacagt atggcctcat tatatatttt gatttatagg agtttgtgtc tgggctcaac 780
atgcta 786

<210> 179
<211> 796
<212> DNA
<213> Homo sapien

<400> 179
tagcatgttg agcccagaca ctggttacaa gaccagacct gcttcctcca tatgtaaaca 60
gcttttaaaa agccagtgaa ccttttttaat actttggcaa ccttctttca caggcaaaga 120
acacccccat ccgccccttg tttggagtgc agagtttggc tttggttctt tgccttgcct 180
ggagtatact tctaattcct gttgtcctgc acaagctgaa taccgagcta cccaccgcca 240
cccaggccag gtttccactc atttattact ttatgtttct gttccattgc tggtccacag 300
aaataagttt tcctttggag gaatgtgatt ataccccttt aatttcctcc ttttgctttt 360
ttttaatatc attggtatgt gtttggccca gaggaaactg aaatttcacca tcatcttgac 420
tggcaatccc attaccatgc ttttttaaa aaacgtaatt tttcttgcct tacattggca 480
gagtagccct tcctggctac tggcttaatg tagtcactca gtttctaggt ggcattaggc 540
atgagacctg aagcacagac tgtcttacca caaaaggtga caagatctca aaccttagcc 600
aaagggctat gtcaggtttc aatgctatct gcttctgttc ctgctcactg ttctggattt 660
tgtccttctt catcccctagc accagaattt cccagtctcc ctccctacct tcccttgttt 720
taattctaat ctatcagcaa aataactttt caaatgtttt aaccggtatc tccatgtgtc 780
tgggctcaac atgcta 796

<210> 180
<211> 488
<212> DNA
<213> Homo sapien

<400> 180
ggatgtgctg caaggcgatt aagttgggta acgccagggt tttcccagtc acgacgttgt 60
aaaacgacgg ccagtgaatt gtaatacgac tcactatagg gcgaattggg cccgacgtcg 120
catgctcccg gccgccatgg ccgcgggata gcatgttgag cccagacacc tgcaggtcat 180
ttggagagat ttttcacgtt accagcttga tggtcttttt caggaggaga gacactgagc 240
actcccaagg tgaggttgaa gatttcctct agatagccgg ataagaagac taggagggat 300
gcctagaaaa tgattagcat gcaaatttct acctgccatt tcagaactgt gtgtcagccc 360
acattcagct gcttcttgtg aactgaaaag agagaggtat tgagactttt ctgatggccg 420
ctctaacatt gtaacacagt aatctgtgtg tgtgtgggtg tgtgtgtgtg tctgggdtca 480
acatgcta 488

<210> 181
<211> 317
<212> DNA
<213> Homo sapien

<400> 181
tagcatgttg agcccagaca cggcgacggt acgtgatgag tggggtgatg gcacctgtga 60
aaaggaggaa cgtcatcccc catgatattg gggacccaga tgatgaacca tggctccgcg 120
tcaatgcata tttaatccat gatactgctg attggaagga cctgaacctg aagtttgtgc 180
tgcaggttta tcgggactat tacctcacgg gtgatcaaaa cttcctgaag gacatgtggc 240
ctgtgtgtct agtaagggat gcacatgcag tggccagtgt gccaggggta tggttggtgt 300
ctgggctcaa catgcta 317

<210> 182
<211> 507
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(507)
<223> n = A,T,C or G

<400> 182
tagcatgttg agcccagaca ctggctgtta gccaaatcct ctctcagctg ctccctgtgg 60
tttggtgact caggattaca gaggcatcct gtttcaggga acaaaaagat tttagctgcc 120
agcagagagc accacatacn ttagaatggt aaggactgcc acctccttca agaacaggag 180
tgagggtggt ggtgaatggg aatggaagcc tgcattcctt gatgcatttg tgctctctca 240
aatcctgtct tagtcttagg aaaggaagta aagtttcaag gacggttccg aactgctttt 300
tgtgtctggg ctcaacatgc tatcccgcgg ccatggcggc cgggagcatg cgacgtcggg 360
cccaattcgc cctatagtga gtcgtattac aattcactgg ccgtcgtttt acaacgtcgt 420
gactgggaaa accctggcgt tacccaactt aatcgccttg cagcacatcc cccttttccca 480
gctggcgtaa tancgaaaag gcccgca 507

<210> 183
<211> 227
<212> DNA
<213> Homo sapien

<400> 183
gatttacgct gcaacactgt ggaggtagcc ctggagcaag gcaggcatgg atgcttctgc 60
aatccccaaa tggagcctgg tatttcagcc aggaatctga gcagagcccc ctctaattgt 120
agcaatgata agttattctc tttgttcttc aaccttccaa tagccttgag cttccagggg 180
agtgtcgtta atcattacag cctggtctcc acagtgttgc agcgtaa 227

<210> 184
<211> 225
<212> DNA
<213> Homo sapien

<400> 184
ttacgctgca acactgtgga gcagattaac atcagacttt tctatcaaca tgactggggt 60
tactaaaaag acaacaaatc aatggcttca aaagtctaag gaataatttc gatacttcaa 120
ctttataaaa cctgacaaaa ctatcaatca agcataaaga cagatgaaga acatttccag 180
attttggcca atcagatatt ttacctccac agtgttgcag cgtaa 225

<210> 185
<211> 597
<212> DNA
<213> Homo sapien

<400> 185
ggcccgacgt cgcatgctcc cggccgccat ggccgcggga ttcgttaggg tctctatcca 60
ctgggaccca taggctagtc agagtattta gagttgagtt cctttctgct tcccagaatt 120
tgaaagaaaa ggagtgaggt gatagagctg agagatcaga tttgcctctg aagcctgttc 180
aagatgtatg tgctcagacc ccaccactgg ggcctgtggg tgaggtcctg ggcatctatt 240
tgaatgaatt gctgaagggg agcactatgc caaggaaggg gaacccatcc tggcactggc 300
acaggggtca ccttatccag tgctcagtgc ttctttgctg ctacctggtt ttctctcata 360
tgtgaggggc aggtaagaag aagtgcccrg tgttgtgcga gttttagaac atctaccagt 420
aagtggggaa gtttcacaaa gcagcagctt tgttttgtgt attttcacct tcagttagaa 480
gaggaaggct gtgagatgaa tgttagttga gtggaaaaga cgggtaagct tagtggatag 540
agaccctaac gaatcactag tgcggccgcc ttgcaggtcg accatatggg agagctc 597

<210> 186
<211> 597
<212> DNA
<213> Homo sapien

<400> 186
ggcccgaagt tgcatgttcc cggccgccat ggccgcggga ttcgttaggg tctctatcca 60
ctacctaaaa aatcccaaac atataactga actcctcaca cccaattgga ccaatccatc 120
accccagagg cctacagatc ctcctttgat acataagaaa atttccccaa actacctaac 180
tatatcattt tgcaagattt gttttaccaa attttgatgg cctttctgag cttgtcagtg 240
tgaaccacta ttacgaacga tcggatatta actgcccctc accgtccagg tgtagctggc 300
aacatcaagt gcagtaaata ttcattaagt tttcacctac taaggtgctt aaacacccta 360
gggtgccatg tcggtagcag atcttttgat ttgtttttat ttccataag ggtcctgttc 420
aaggtcaatc atacatgtag tgtgagcagc tagtcactat cgcatgactt ggagggtgat 480
aatagaggcc tcctttgctg ttaaagaact cttgtcccag cctgtcaaag tggatagaga 540
ccctaacgaa tcactagtgc ggccgcctgc aggtcgacca tatgggagag ctcccaa 597

<210> 187
<211> 324
<212> DNA

<213> Homo sapien

<400> 187
tcgttagggt ctctatccac ttgcaggtaa aatccaatcc tgtgtatatc ttatagtctt 60
ccatatgtag tggttcaaga gactgcagtt ccagaaagac tagccgagcc catccatgtc 120
ttccacttaa ccctgctttg ggttacacat cttaactttt ctgttcaagt ttctctgtgt 180
agtttatagc atgagtattg ggawaatgcc ctgaaacctg acatgagatc tgggaaacac 240
aaacttactc aataagaatt tctcccatat ttttatgatg gaaaaatttc acatgcacag 300
aggagtggat agagacccta acga 324

<210> 188
<211> 178
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(178)
<223> n = A,T,C or G

<400> 188
gcgcggggat tcggggtgat acctcctcat gccaaaatac aacgtntaat ttcacaactt 60
gccttccaat ttacgcattt tcaatttgct ctccccattt gttgagtcac aacaaacacc 120
attgcccaga aacatgtatt acctaacatg cacatactct taaaactact catccctt 178

<210> 189
<211> 367
<212> DNA
<213> Homo sapien

<400> 189
tgacaccttg tccagcatct gacacagtct tggctcttgg aaaatattgg ataaatgaaa 60
atgaatttct ttagcaagtg gtataagctg agaatatacg tatcacatat ccttattcta 120
agacacattc agtgtccctg aaattagaat aggacttaca ataagtgtgt tcactttctc 180
aatagctgtt attcaattga tggtaggcct taaaagtcaa agaaatgaga gggcatgtga 240
aaaaaagctc aacatcactg atcattagaa aacttccatt caaaccccca atgagatacc 300
atctcatacc agtcagaatg gctattatta aaaagtcaaa aaataacaga tgctggacaa 360
ggtgtca 367

<210> 190
<211> 369
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(369)
<223> n = A,T,C or G

<400> 190
gacaccttgt ccaggatctg acaacgctaa cagcctgagg agatctttat ttatttattt 60
agtttttact ctggctaggc agatggtggc taaaacattc atttacccat ttattcattt 120
aattgttcct gcaaggccta tggatagagt attgtccagc actgctctgg aagctaggag 180
catggggatg aacaagatag gctacatcct gttcccacag aacttccact ttagtctggg 240
aaacagatga tatatacaaa tatataaatg aattcaggta gttttaagta cgaaaagaat 300

aagaaagcag agtcatgatt tanaatgctg gaaacagggg ctattgcttg agatattgaa 360
ggtgcccaa 369

<210> 191
<211> 369
<212> DNA
<213> Homo sapien

<400> 191
tgacaccttg tccagcatct gcacagggaa aagaaactat tatcagagtg aacaggcaac 60
ctacagaatg ggagaaaatt tttgcaatct atccatctga caaagggcta atatccagaa 120
tctacaaaga acttatacaa atttacaaga aacaaacaaa caaacaactc ctcaaaaagt 180
gggtgaagga tgtgaacaga cacttctcaa aagaagacat ttatggggcc aacaaacata 240
tgaaaaaaag ctcatcatca ctggtcacta gataaatgca aatcaaaacc acaatgagat 300
accatctcat tccagttaga atggcaatca ttaaaaagtc aggaaacaac agatgctgga 360
caaggtgtc 369

<210> 192
<211> 449
<212> DNA
<213> Homo sapien

<400> 192
tgacgcttgg ccacttgaca cttcatcttt gcacagaaaa acttctttac agatttaatt 60
caagactggt ctagtgacag tcctccagac atttttttcat ttgttccata tacgtggaat 120
tttaaaatca tgtttcatca gtttgaaatg atttgggctg ctaatcaaca caattggatc 180
gactgttcta ctaaacaaca ggaaaatgtg tatctggcag cctgtggaga aacactaaac 240
attgattttt ctttgccttt tacggacttt gttccagcta catgtaatac caagttctct 300
ttaagaggag aagatgttga tcttcatttg tttctaccag actgccaccc tagtaaatat 360
tctttattta tgctggtaaa aaattgccat ccaaataaga tgattcatga tactggtatt 420
cctgctgagt gtcaagtggc caagcgtca 449

<210> 193
<211> 372
<212> DNA
<213> Homo sapien

<400> 193
tgacgcttgg ccacttgaca ccagggatgt akcagttgaa tataatcctg caattgtaca 60
tattggcaat ttcccatcaa acattctaga aagagacaac caggattgct aggccataaa 120
agctgcaata aataactggt aattgcagta atcatttcag gccaattcaa tccagtttgg 180
ctcagaggtg cctttggctg agagaagagg tgagatataa tgtgttttct tgcaacttct 240
tggaagaata actccacaat agtctgagga ctagatacaa acctatttgc cattaaagca 300
ccagagtctg ttaattccag tactgataag tgttggagat tagactccag tgtgtcaagt 360
ggccaagcgt ca 372

<210> 194
<211> 309
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(309)
<223> n = A,T,C or G

<400> 194
tgacgcttgg ccacttgaca cttatgtaga atccatcgtg ggctgatgca agccctttat 60
ttaggcttag tgttgtgggc accttcaata tcacactaga gacaaacgcc acaagatctg 120
cagaaacatt cagttctgan cactcgaatg gcaggataac tttttgtgtt gtaatccttc 180
acatatacaa aaacaaactc tgcantctca cgttacaaaa aaacgtactg ctgtaaaata 240
ttaagaaggg gtaaaggata ccatctataa caaagtaact tacaactagt gtcaagtggc 300
caagcgtca 309

<210> 195
<211> 312
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(312)
<223> n = A,T,C or G

<400> 195
tgacgcttgg ccacttgaca cccaatctcg cacttcatcc tcccagcacc tgatgaagta 60
ggactgcaac tatccccact tcccagatga ggggaccaan gtacacatta ggacccggat 120
gggagcacag atttgtccga tcccagactc caagcactca gcgtcactcc aggacagcgg 180
ctttcagata aggtcacaaa catgaatggc tccgacaacc ggagtcagtc cgtgctgagt 240
taaggcaatg gtgacacgga tgcacgtgtn acctgtaatg gttcatcgta agtgtcaagt 300
ggccaagcgt ca 312

<210> 196
<211> 288
<212> DNA
<213> Homo sapien

<400> 196
tgtatcgacg tagtggtctc ctcagccatg cagaactgtg actcaattaa acctctttcc 60
tttatgaatt acccaatctc gggtagtgtc tttatagtag tgtgagaatg gactaataca 120
agtacatttt acttagtaat aataataaac aaatatatta cattttgtg tatttactac 180
accatatttt ttattgttat tgtagtgtac accttctact tattaaaaga aataggcccg 240
aggcgggcag atcacgaggt caggagatgg agaccactac gtcgatac 288

<210> 197
<211> 289
<212> DNA
<213> Homo sapien

<400> 197
ttgggcacct tcaatatcat gacaggtgat gtgataacca agaaggctac taagtgatta 60
atgggtgggt aatgtataca gagtaggtac actggacaga ggggtaattc atagccaagg 120
caggagaagc agaatggcaa aacatttcat cacactactc aggatagcat gcagtttaaa 180
acctataagt agtttatttt tggaattttc cacttaatat tttcagactg caggtaacta 240
aactgtggaa cacaagaaca tagataaggg gagaccacta cgtcgatac 289

<210> 198
<211> 288
<212> DNA
<213> Homo sapien

<400> 198
gtatcgacgt agtggtctcc caagcagtgg gaagaaaacg tgaaccaatt aaaatgtatc 60
agataccca aagaaaggcg cttgagtaaa gattccaagt gggtcacaat ctcagatctt 120
aaaattcagg ctgtcaaaga gatttgctat gaggttgctc tcaatgactt caggcacagt 180
cggcaggaga ttgaagccct ggccattgtc aagatgaagg agctttgtgc catgtatggc 240
aagaaagacc ccaatgagcg ggactcctgg agaccactac gtcgatac 288

<210> 199
<211> 1027
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(1027)
<223> n = A,T,C or G

<400> 199
gctttttggg aaaaacncaa ntgggggaaa gggggnttnn tngcaagggg ataaaggggg 60
aancccaggg tttccccatt cagggaggtg taaaaagncg gccaggggat tgtaanagga 120
ttcaataata gggggaatgg gcccngaagt tgcaaggttc cngcccgcca tgnccgcggg 180
atttagtgac attacgacgs tggtaataaa gtgggsccaa waaatatttg tgatgtgatt 240
tttsgaccag tgaacccatt gwacaggacc tcatttccty tgagatgrta gccataatca 300
gataaaagrt tagaagtytt tctgcacgtt aacagcatca ttaaatggag tggcatcacc 360
aatttcaccc tttgttagcc gataccttcc ccttgaaggc attcaattaa gtgaccaatc 420
gtcatacgag aggggatggc atggggattg atgatgatat caggggtgat accttcacag 480
gtgaaaggca tatcctcttg tctatactga ataccacaag tacccttttg accatgtcga 540
ctagcaaatt tgtctccaat ctgtgtwatc cctaacagag cgtaccctta ttttacaaaa 600
tttatatcct tcctgattga cagttaccat aacctgatcc acaatgcccg tctcgctwgt 660
tctgagaaaa gtgctacagt ctctcttggt atagcgtcta ttggtgctct ccaattcatc 720
ttcatttttc aggcaaggtg aactgttttt cctatactaa cmtcatctcc tgatacmcga 780
aacccckgga rctatcaaac catcatcatc gcgttckt watgtymcta aatccctatt 840
gcggccgcct gcaggtcaac atatnggaaa acccccccacc ccttnggagc ntaccttgaa 900
ttttccatat gtcccntaaa ttanctngnc ttancctggc cntaacctnt tccggtttaa 960
attgtttccg cccccnttcc ccncctttnna accggaaacc ttaattttna accnggggtt 1020
cctatcc 1027

<210> 200
<211> 207
<212> DNA
<213> Homo sapien

<400> 200
agtgacatta cgacgctggc catcttgaat cctagggcat gaagttgccc caaagttcag 60
cacttggtta agcctgatcc ctctggttta tcacaaagaa taggatggga taaagaaagt 120
ggacacttaa ataagctata aattatatgg tccttgtcta gcaggagaca actgcacagg 180
tatactacca gcgtcgtaat gtcacta 207

<210> 201
<211> 209
<212> DNA
<213> Homo sapien

<400> 201

tgggcacctt caatatctat taaaagcaca aatactgaag aacacaccaa gactatcaat 60
gaggttacat ctggagtcct cgatatatca ggaaaaaatg aagtgaacat tcacagagtt 120
ttacttcttt gggaactcaa atgctagaaa agaaaagggt gccctctttc tctggcttcc 180
tggtcctatc cagcgtcgta atgtcacta 209

<210> 202
<211> 349
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(349)
<223> n = A,T,C or G

<400> 202
ntacgctgca acactgtgga gccactggtt tttattcccg gcaggttatc cagcaaacag 60
tcactgaaca caccgaagac cgtggtatgg taaccgttca cagtaatcgt tccagtcgtc 120
tgcgggaccc cgacgagcgt cactgggtac agaccagatt cagccggaag agaaagcgcc 180
gcagggagag actcgaactc cactccgctg gtgagcagcc ccatgttttc aactcgaagt 240
tcaaacggca ttgggttata taccatcagc tgaacttcac acacatctcc ttgaaccgac 300
tggaaatcta ttttcttgtt ccgctctttc ccacagtgtt gcagcgaau 349

<210> 203
<211> 241
<212> DNA
<213> Homo sapien

<400> 203
tgctcctctt gccttaccaa cccaaagccc actgtgaaat atgaagtgaa tgacaaaatt 60
cagttttcaa cgcaatatag tatagtttat ctgattcttt tgatctccag gacactttaa 120
acaactgcta ccaccaccac caacctaggg tatttaggatt ctccacagac cagaaattat 180
ttctcctttg agtttcaggc tcctctggga ctcctgttca tcaatgggtg gtaaatggct 240
a 241

<210> 204
<211> 248
<212> DNA
<213> Homo sapien

<400> 204
tagccattta ccacccatct gcaaaccswg acmwwcargr cywgwackya ggcgatttga 60
agtactggta atgctctgat catgttagtt acataagtgt ggtcagttta caaaaattca 120
cagaactaaa tactcaatgc tatgtgttca tgtctgtgtt tatgtgtgtg taatgtttca 180
attaagtttt tttaaaaaaa agagatgatt tccaaataag aaagccgtgt tggtaaggca 240
agaggagc 248

<210> 205
<211> 505
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(505)

<223> n = A,T,C or G

<400> 205

tacgctgcaa cactgtggag ccattcatac aggtccctaa ttaaggaaca agtgattatg 60
ctacctttgc acggttaggg taccgcggcc gttaaacatg tgtcactggg caggcggtgc 120
ctctaatact ggtgatgcta gaggtgatgt ttttggtaaa caggcggggt aagatttgcc 180
gagttccttt tacttttttt aacctttcct tatgagcatg cctgtgttgg gttgacagtg 240
ggggtaataa tgacttgttg gttgattgta gatattgggc tgttaattgt cagttcagtg 300
ttttaatctg acgcaggctt atgcggagga gaatgttttc atgttactta tactaacatt 360
agttcttcta tagggtgata gattggtcca attgggtgtg aggagttcag ttatatgttt 420
gggatttttt aggtagtggg tgttganctt gaacgctttc ttaattggtg gctgctttta 480
rgcctactat gggtggtaaa tggct 505

<210> 206
<211> 179
<212> DNA
<213> Homo sapien

<400> 206

tagactgact catgtcccct accaaagccc atgtaaggag ctgagttctt aaagactgaa 60
gacagactat tctctggaga aaaataaaat ggaaattgta ctttaaaaaa aaaaaaaatc 120
ggccgggcat ggtagcacac acctgtaatc ccagctacta ggggacatga gtcagtcta 179

<210> 207
<211> 176
<212> DNA
<213> Homo sapien

<400> 207

agactgactc atgtcccctа ccccaccttc tgctgtgctg ccgtgttcct aacaggtcac 60
agactggtac tggtcagtgg cctgggggtt ggggacctct attatatggg atacaaattt 120
aggagttgga attgacacga tttagtgact gatgggatat gggtggtaaa tggcta 176

<210> 208
<211> 196
<212> DNA
<213> Homo sapien

<400> 208

agactgactc atgtcccctа tttaacaggg tctctagtgc tgtgaaaaaa aaaaatgctg 60
aacattgcat ataacttata ttgtaagaaa tactgtacaa tgactttatt gcatctgggt 120
agctgtaagg catgaaggat gccaagaagt ttaaggaata tgggtggtaa atggctaggg 180
gacatgagtc agtcta 196

<210> 209
<211> 345
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(345)
<223> n = A,T,C or G

<400> 209

gacgcttggc cacttgacac cttttatttt ttaaggattc ttaagtcatt tangtnactt 60
tgtaagtttt tcctgtgccc ccataagaat gatagcttta aaaattatgc tggggtagca 120
aagaagatac ttctagcttt agaatgtgta ggtatagcca ggattcttgt gaggaggggt 180
gatttagagc aaatttctta ttctccttgc ctcatctgta acatggggat aataatagaa 240
ctggcttgac aaggttggaa ttagtattac atggtaaata catgtaaaat gtttagaatg 300
gtgccaagta tctaggaagt acttgggcat gggtggtaaa tggct 345

<210> 210
<211> 178
<212> DNA
<213> Homo sapien

<400> 210
gacgcttggc cacttgacac tagagtaggg tttggccaac tttttctata aaggaccaga 60
gagtaaatat ttcaggcttt gtgggttgtg cagtctctct tgcaactact cagctctgcc 120
attgtagcat agaaatcagc catagacagg acagaaatga atgggtggta aatggcta 178

<210> 211
<211> 454
<212> DNA
<213> Homo sapien

<400> 211
tgggcacctt caatatctat ccagcgcatc taaattcgct tttttcttga ttaaaaattt 60
caccacttgc tgtttttgct catgtatacc aagtagcagt ggtgtgaggc catgcttgtt 120
ttttgattcg atatcagcac cgtataagag cagtgctttg gccattaatt tatcttcatt 180
gtagacagca tagtgtagag tggtatctcc atactcatct ggaatatttg gatcagtgcc 240
atgttccagc aacattaacg cacattcatc ttcctggcat tgtacggcct ttgtcagagc 300
tgtcctcttt ttgttgtcaa ggacattaag ttgacatcgt ctgtccagca cgagttttac 360
tacttctgaa ttccattgg cagaggccag atgtagagca gtcctctttt gcttgtccct 420
cttgttcaca tcagtgtccc tgagcataac ggaa 454

<210> 212
<211> 337
<212> DNA
<213> Homo sapien

<400> 212
tccgttatgc cacccagaaa acctactgga gttacttatt aacatcaagg ctggaaccta 60
tttgcctcag tcctatctga ttcatgagca catggttatt actgatcgca ttgaaaacat 120
tgatcacctg ggtttcttta tttatcgact gtgtcatgac aaggaaactt acaaactgca 180
acgcagagaa actattaaag gtattcagaa acgtgaagcc agcaattgtt tcgcaattcg 240
gcattttgaa aacaaatttg ccgtggaaac tttaatttgt tcttgaacag tcaagaaaaa 300
cattattgag gaaaattaat atcacagcat aacggaa 337

<210> 213
<211> 715
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(715)
<223> n = A,T,C or G

<400> 213
tcgggtgatg cctcctcagg catcttccat ccatctcttc aagattagct gtcccaaatg 60
ttttttcctc tcttctttac tgataaattt ggactccttc ttgacactga tgacagcttt 120
agtatccttc ttgtcacctt gcagacttta aacataaaaa tactcattgg ttttaaaagg 180
aaaaaagtat acattagcac tattaagctt ggccttgaaa cattttctat cttttattaa 240
atgtcggtta gctgaacaga attcatttta caatgcagag tgagaaaaga agggagctat 300
atgcatttga gaatgcaagc attgtcaaat aaacatttta aatgctttct taaagtgagc 360
acatacagaa atacattaag atattagaaa gtgtttttgc ttgtgtacta ctaattaggg 420
aagcaccttg tatagttcct cttctaaaat tgaagtagat tttaaaaacc catgtaattt 480
aattgagctc tcagttcaga ttttaggaga attttaacag ggatttggtt ttgtctaaat 540
tttgtcaatt tntttagtta atctgtataa ttttataaat gtcaaactgt atttagtccg 600
ttttcatgct gctatgaaag aaatacccan gacagggtta tttataaang gaaagangtt 660
aatttgactc ccagttcaca ggcctgagga ngnatcnccc gaaatcctta ttgcg 715

<210> 214
<211> 345
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)..(345)
<223> n = A,T,C or G

<400> 214
ggtaangngc atacntcggt gctccggccg ccggagtcgg gggattcggg tgatgcctcc 60
tcaggcccac ttgggcctgc ttttcccaaa tggcagctcc tctggacatg ccattccttc 120
tcccacctgc ctgattcttc atatgttggg tgtccctgtt tttctggtgc tatttcctga 180
ctgctgttca gctgccactg tcctgcaaag cctgcctttt taaatgcctc accattcctt 240
catttgtttc ttaaatatgg gaagtgaaag tgccacctga ggccgggcac agtggctcac 300
gcctgtaatc ccagcacttt gggagcctga ggaggcatca cccga 345

<210> 215
<211> 429
<212> DNA
<213> Homo sapien

<400> 215
ggtgatgcct cctcaggcga agctcaggga ggacagaaac ctcccgtgga gcagaagggc 60
aaaagctcgc ttgatcttga ttttcagtac gaatacagac cgtgaaagcg gggcctcacg 120
atccttctga ccttttgggt tttaagcagg aggtgtcaga aaagttacca cagggataac 180
tggcttgtgg cggccaagcg ttcatagcga cgtcgctttt tgatccttcg atgtcggctc 240
ttcctatcat tgtgaagcag aattcaccaa gcgttggatt gttcacccac taatagggaa 300
cgtgagctgg gtttagaccg tcgtgagaca ggttagtttt accctactga tgatgtgtkg 360
ttgccatggt aatcctgctc agtacgagag gaaccgcagg ttcasacatt tggtgtatgt 420
gcttgcctt 429

<210> 216
<211> 593
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)..(593)

<223> n = A,T,C or G

<400> 216

tgacacctat gtccngcatc tgttcacagt ttccacaaat agccagcctt tggccacctc 60
tctgtcctga ggtatacaag tatatcagga ggtgtatacc ttctcttctc ttccccacca 120
aagagaacat gcaggctctg gaagctgtct taggagcctt tgggctcaga atttcagagt 180
cttgggtacc ttggatgtgg tctggaagga gaaacattgg ctctggataa ggagtacagc 240
cggaggaggg tcacagagcc ctcagctcaa gcccctgtgc cttagtctaa aagcagcttt 300
ggatgaggaa gcaggttaag taacatacgt aagcgtacac aggtagaaag tgctgggagt 360
cagaattgca cagtgtgtag gagtagtacc tcaatcaatg agggcaaatc aactgaaaga 420
agaagaccna ttaatgaatt gcttangggg aaggatcaag gctatcatgg agatctttct 480
aggaagatta ttgtttanaa ttatgaaagg antagggcag ggacagggcc agaagtanaa 540
ganaacattg cctatanccc ttgtcttgca cccagatgct ggacaaggtg tca 593

<210> 217
<211> 335
<212> DNA
<213> Homo sapien

<400> 217

tgacaccttg tccagcatct gacgtgaaga tgagcagctc agaggaggtg tcctggattt 60
cctggttctg tgggctccgt ggcaatgaat tcttctgtga agtggatgaa gactacatcc 120
aggacaaatt taatcttact ggactcaatg agcaggtccc tcactatcga caagctctag 180
acatgatctt ggacctggag cctgatgaag aactggaaga caaccccaac cagagtgacc 240
tgattgagca ggcagccgag atgctttatg gattgatcca cgcccgctac atccttacca 300
accgtggcat cgcccagatg ctggacaagg tgtca 335

<210> 218
<211> 248
<212> DNA
<213> Homo sapien

<400> 218

tacgtactgg tcttgaaggt cttaggtaga gaaaaaatgt gaatatttaa tcaaagacta 60
tgtatgaaat gggactgtaa gtacagaggg aagggtggcc cttatcgcca gaagttggta 120
gatgcgtccc cgtcatgaaa tgttgtgtca ctgcccgaca tttgccgaat tactgaaatt 180
ccgtagaatt agtgcaaatt ctaacgttgt tcatctaaga ttatggttcc atgtttctag 240
tactttta 248

<210> 219
<211> 530
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(530)
<223> n = A,T,C or G

<400> 219

tgacgcttgg ccacttgaca caagtagggg ataaggacaa agacccatna ggtggcctgt 60
cagccttttg ttactgttgc ttccctgtca ccacggcccc ctctgtaggg gtgtgctgtg 120
ctctgtggac attggtgcat tttcacacat accattctct ttctgcttca cagcagtcct 180
gaggcgggag cacacaggac taccttgtca gatgangata atgatgtctg gccaactcac 240
cccccaacct tctcactagt tatangaaga gccangccta nnaccttcta tcctgncccc 300

ttgccctatg acctcatccc tgttccatgc cctattctga tttctggtga actttggagc 360
agcctggttt ntcctcctca ctccagcctc tctccatacc atggtanggg ggtgctgttc 420
cacncaaang gtcaggtgtg tctggggaat cctnananct gccnggagtt tccnangcat 480
tcttaaaaac cttcttgcct aatcanatng tgtccagtgg ccaaccntcn 530

<210> 220
<211> 531
<212> DNA
<213> Homo sapien

<400> 220
tgacgcttgg ccacttgaca ctaaatagca tcttctaaag gcctgattca gagttgtgga 60
aaattctccc aytgtcaggg attgtcagga acagggctgc tcctgtgctc actttacctg 120
ctgtgtttct gctggaaaag gagggaagag gaatggctga tttttaccta atgtctccca 180
gttttttcata ttcttcttgg atcctcttct ctgacaactg ttccctttg gtcttcttct 240
tcttgctcag agagcaggtc tctttaaaac tgagaaggga gaatgagcaa atgattaaag 300
aaaacacact tctgaggccc agagatcaaa tattaggtaa atactaaacc gcttgcctgc 360
tgtggtcact tttctcctct ttcacatgct ctatccctct atcccccacc tattcatatg 420
gcttttatct gccnagttat ccggcctctc atcaaccttc tcccctagcc tactgggggga 480
tatccatctg ggtctgtctc tggtgtattg gtgtcaagtg gccaagcgtc a 531

<210> 221
<211> 530
<212> DNA
<213> Homo sapien

<400> 221
attgacgctt ggccacttga cacccgcctg cctgcaatac tggggcaagg gccttcactg 60
ctttcctgcc accagctgcc actgcacaca gagatcagaa atgctaccaa ccaagactgt 120
tggtcctcag cctctctgag gagaaagagc agaagcctgg aagtcagaag agaagctaga 180
tcggctacgg ccttggcagc cagcttcccc acctgtggca ataaagtcgt gcatggctta 240
acaatggggg cacctcctga gaaacacatt gttaggcaat tcggcgtgtg ttcatcagag 300
catatttaca caaacctcga tagtgcagcc tactatccac tattgctcct acgctgcaaa 360
cctgaacagc atgggactgt actgaatact ggaagcagct ggtgatggta cttatttgtg 420
tatctaaaca cagagaaggt acagtaagaa tatggtatca taaacttaca gggaccgcca 480
tcctatatgc agtctgttgt gaccaaaatg tgtcaagtgg ccaagcgtca 530

<210> 222
<211> 578
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(578)
<223> n = A,T,C or G

<400> 222
tgtatcgacg tagtggtctc cgggctacta ggccgttgtg tgctggtagt acctggttca 60
ctgaaaggcg catctccctc cccgcgtcgc cctgaagcag ggggaggact tcgcccagcc 120
aaggcagttg tatgagtttt agctgcggca cttcgagacc tctgagccca cctccttcag 180
gagccttccc cgattaagga agccagggta aggattcctt cctcccccag acaccacgaa 240
caaaccacca ccccccctat tctggcagcc catatacatc agaacgaaac aaaaataaca 300
aataaacnaa aaccaaaaaa aaaagagaag gggaaatgta tatgtctgtc catcctgttg 360
ctttagcctg tcagctccta nagggcaggg accgtgtctt ccgaatggtc tgtgcagcgc 420

cgactgcggg aagtatcgga ggaggaagca gagtcagcag aagttgaacg gtgggcccgg 480
cggctcttgg gggctggtgt tgtacttcga gaccgctttc gctttttgtc ttagatttac 540
gtttgctctt tggagtggga naccactacn tcnataca 578

<210> 223
<211> 578
<212> DNA
<213> Homo sapien

<400> 223
tgtatcgacg tagtggtctc ctcttgcaaa ggactggctg gtgaatggtt tccctgaatt 60
atggacttac cctaaacata tcttatcatc attaccagtt gcaaaatatt agaatgtgtt 120
gtcactgttt catttgattc ctagaaggtt agtcttagat atgttacttt aacctgtatg 180
ctgtagtgct ttgaatgcat tttttgtttg cattttgttt tgcccaacct gtcaattata 240
gctgcttagg tctggactgt cctggataaa gctgttaaaa tattcaccag tccagccatc 300
ttacaagcta attaagtcaa ctaaatgctt ccttgttttg ccagacttgt tatgtcaatc 360
ctcaatttct gggttcattt tgggtgccct aaatcttagg gtgtgacttt cttagcatcc 420
tgtaacatcc attcccaagc aagcacaact tcacataata ctttccagaa gttcattgct 480
gaagcctttc cttcacccag cggagcaact tgatttttta caacttccct catcagagcc 540
acaagagtat gggatatgga gaccactacg tcgataca 578

<210> 224
<211> 345
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)..(345)
<223> n = A,T,C or G

<400> 224
tgtatcgacg tantggtctc ccaaggtgct gggattgcag gcatgagcca ccactcccag 60
gtggatcttt ttctttatac ttacttcatt agcttctgt tattcaagaa gtgtagtggt 120
aaaagtcttt tcaatctaca tggttaaata atgatagcct gggaaataaa tagaaatttt 180
ttctttcatc tttaggttga ataaacaaac agaaaaaata gaacatactg aaaataatct 240
aagttccaac catagaagaa ctgcagaaga aatgaagaaa gtgatgatga tttagatttt 300
gatattgatt tagaagacac aggaggagac cactacgtcg ataca 345

<210> 225
<211> 347
<212> DNA
<213> Homo sapien

<400> 225
tgtatcgacg tagtggtctc caaactgagg tatgtgtgcc actagcacac aaagccttcc 60
aacagggacg caggcacagg cagtttaaag ggaatctgtt tctaaattaa tttccacctt 120
ctctaagtat tctttcctaa aactgatcaa ggtgtgaagc ctgtgctctt tcccaactcc 180
cctttgacaa cagccttcaa ctaacacaag aaaaggcatg tctgacactc ttcctgagtc 240
tgactctgat acgttgttct gatgtctaaa gagctccaga acaccaaagg gacaattcag 300
aatgctggtg tataacagac tccaatggag accactacgt cgataca 347

<210> 226
<211> 281
<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)..(281)

<223> n = A,T,C or G

<400> 226

aggngnggga ntgtatcgac gtagtggtct cccaacagtc tgtcattcag tctgcaggtg 60
tcagtgttct ggacaatgag gcaccattgt cacttattga ctcctcagct ctaaatgctg 120
aaattaaatc ttgtcatgac aagtctggaa ttcctgatga ggtttttacaa agtattttgg 180
atcaatactc caacaaatca gaaagccaga aagaggatcc tttcaatatt gcagaaccac 240
gagtggattt acacacctca ggagaccact acgtcgatac a 281

<210> 227

<211> 3646

<212> DNA

<213> Homo sapien

<400> 227

gggaaacact tcctcccagc cttgtaaggg ttggagccct ctccagtata tgctgcagaa 60
tttttctctc ggtttctcag aggattatgg agtccgcctt aaaaaaggca agctctggac 120
actctgcaaa gtagaatggc caaagtttgg agttgagtgg ccccttgaag ggtcactgaa 180
cctcacaatt gttcaagctg tgtggcgggt tgttactgaa actcccggcc tccctgatca 240
gtttccctac attgatcaat ggctgagttt ggtcaggagc acccccttccg tggctccact 300
catgcaccat tcataatttt acctccaagg tcctcctgag ccagaccgtg ttttcgcctc 360
gaccctcagc cggttcggct cgccctgtac tgcctctctc tgaagaagag gagagtctcc 420
ctcacccagt cccaccgcct taaaaccagc ctactccctt agggtcatcc catgtctcct 480
cggctatgtc ccctgtaggc tcatcaccca ttgcctcttg gttgcaaccg tggtgggagg 540
aagtagcccc tctactacca ctgagagagg cacaagtccc tctgggtgat gagtgctcca 600
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aatcctccct tctctgaaaa gccccaggct ttgacctcac tgatggagtc tgtactctgg 720
acacattggc ccacctggga tgactgtcaa cagctccttt tgacccttt cacctctgaa 780
gagagggaaa gtatccaaag agaggccaaa aagtacaacc tcacatcaac caataggccg 840
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acagtagcag cttcctcgag aagggactac gaaaggccgg tgcagctgtt accatggaga 1560
cagatgtgtt gtgggctcag gctttaccag caaacacctc agcacaaaag gctgaattga 1620
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aacttgctgc ccacagtctc ctttccacag ccagatctgc ctgacaatcc cgcatactca 1920
acagaagaag aaaactggcc tcagaactca gagccaataa aaatcaggaa ggttggtgga 1980
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agatccccca tcttcaaagc ctaacagatc aagcagctct ccggtgcaca acctgcgccc 2160
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ccccaacagg tacaagatat catcctgcca cttgttcgag gaaccatcc caatccaatt 2820
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acggctctga aggtggatgg cattcctgcg tggattcatc actcccgcat caaaaaggcc 3000
aacagagccc aactagaaac atgggtcccc agggctgggt caggcccctt aaaactgcac 3060
ctaagttggg tgaagccatt agattaattc tttttcttaa ttttgtaaaa caatgcatag 3120
cttctgtcaa acttatgtat cttaagactc aatataaccc ccttgttata actgaggaat 3180
caatgatttg attcccccaa aaacacaagt ggggaatgta gtgtccaacc tggtttttac 3240
taaccctgtt tttagactct ccctttcctt taatcactca gcttgtttcc acctgaattg 3300
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ttcctcaagg acttaacttg tgcaagctga ctcccagcac atccaagaat gcaattaact 3420
gataagatac tgtggcaagc tatatccgca gttcccagga attcgtccaa ttgatcacag 3480
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<210> 228
<211> 419
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(419)
<223> n = A,T,C or G

<400> 228
taagagggta caagatctaa gcacagccgt caatgcagaa cacagaacgt agcctggtaa 60
gtgtgttaag agtgggaatt tttggagtac agagtaaggc acctaaccct agctggggtt 120
tggtgacggt cccagatggc ttacagaaga aagtgtcctg agatgagttt ttaagaatga 180
ataaggatag acacaagtga ggactgactt ggcagtggtg aatggtgggt ggcaaaaaac 240
ttcgcatgta tggaaactgc acgtacagga atgaagaatg agactgtgtg gtgtttaatg 300
agctgcaaat actaatttta tcctgaaagt tttgaagagt taactaaaaa gtatttttta 360
gtaaggaaat aaccctacat ttcagggtta ttgtttgttt anatattgaa ggtgcccaa 419

<210> 229
<211> 148
<212> DNA
<213> Homo sapien

<400> 229
aagagggtac ctgtatgtag ccatggtggc aatgagagac tgattactac ctgctggaga 60
ttgtttaagt gagttaatat attaaggata aagggagcca ggtttttga ctgttggaga 120
aggaaattac agatattgaa ggtcccaa 148

<210> 230
<211> 257
<212> DNA
<213> Homo sapien

<400> 230
taagagggta cmaaaaaaaa aaaatagaac gaatgagtaa gacctactat ttgatagtac 60
aacagggtga ctatagtcaa tgataactta attatacatt taacatagag tgtaattgga 120
ttgtttgtaa ctcgaaggat aaatgcttga gaggatggat accccattct ccatgatgta 180
cttatttcac attacatgcc tgtatcaaag catctcatat accctataaa tatgtacacc 240
tactatgtac cctctta 257

<210> 231
<211> 260
<212> DNA
<213> Homo sapien

<400> 231
taagagggta cgggtatttg ctgatgggat ttttttttct ttctttttct ttggaaaaca 60
aaatgaaagc cagaaccaaa ttattgaaca aaagacaggg actaaatctg gagaaatgaa 120
gtcccctcac ctgactgcca tttcattcta tctcaccttc cagtctaggt taggagaata 180
gggggtggag gggattcatc tgatacaggt atatttaaag caactctgca tgtgtgccag 240
aagtccatgg tcccctctta 260

<210> 232
<211> 596
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(596)
<223> n = A,T,C or G

<400> 232
tgctcctctt gccttaccaa ccacaaatta gaaccataat gagatgtcac ctcatacctg 60
gtgggattaa cattatttaa aaaatcagaa gtattgacaa ggatgtgaag aaattagaac 120
atctgtgcac tgttggtggg aatgtaaaan nggtgtgggc actatgggta acagcatgaa 180
ggttcctcaa aaaaaatttt ttttaatcta ctctatgatc gatcttgagg ttgtttatgc 240
aaaagaactg aaatcaggat tttgaggaaa tattcacctt cccacatcca tttctgcttt 300
attcataata ctgaagagat ggaaacancc taaatgtccn tcccgggatg aatggataaa 360
cacagtgtgg tatatgcata caatggaata ttatttagtc tttaaaanga aaaattctat 420
catatactac aacttanatn aaccttgagg acacaatgct nagtgaaata agccacggaa 480
ggacgaatac tgcattattc ccttatatga agtatctaaa gtggtcaaac tcttanagca 540
naaagtaaaa atgggtggtt gccanacagt tggttaggcn agaaganaan cctant 596

<210> 233
<211> 96
<212> DNA
<213> Homo sapien

<400> 233
tcttctgaag acctttcgcg actcttaagc tcgtggttgg taaggcaaga ggagcgttgg 60
taaggcaaga ggagcgttgg taaggcaaga ggagca 96

<210> 234
<211> 313
<212> DNA
<213> Homo sapien

<400> 234
tgtaagtcga gcagtgtgat gataaaactt gaatggatca atagttgctt cttatggatg 60
agcaaagaaa gtagtttctt gtgatggaat ctgctcctgg caaaaatgct gtgaacgttg 120
ttgaaaagac aacaaagagt ttagagtagt acataaattt agaatagtac ataaacttag 180
aatagtacat aaacttagta cataaataat gcacgaagca ggggcagggc ttgagagaat 240
tgacttcaat ttggaaagag tatctactgt aggttagatg ctctcaaaca gcatcacact 300
gctcgactta caa 313

<210> 235
<211> 550
<212> DNA
<213> Homo sapien

<400> 235
aacgaggaca gatccttaaa aagaatgttg agtgaaaaaa gtagaaaata agataatctc 60
caaagtccag tagcattatt taaacatttt caaaaaatac actgataaaa attttgtaca 120
tttcccaaaa atacatatgg aagcacagca gcatgaatgc ctatgggrtt gaggataggg 180
gttgggagta gggatgggga taaaggggga aaataaaacc agagaggagt cttacacatt 240
tcatgaacca aggagtataa ttatttcaac tatttgtacc wgaagtccag aaagagtgga 300
ggcagaaggg ggagaagagg gcgaagaaac gtttttggga gaggggtccc asaagaggga 360
ttttcgcgat gtggcgctac atacgttttt ccaggatgcc ttaagctctg caccctattt 420
ttctcatcac taatattaga ttaaaccctt tgaagacagc gtctgtggtt tctctacttc 480
agctttccct ccgtgtcttg cacacagtag ctgttttaca agggttgaac tgactgaagt 540
gagattattc 550

<210> 236
<211> 325
<212> DNA
<213> Homo sapien

<400> 236
tagactgact catgtccect atcagagtag ctagaattaa tagcacaagc ctctacacca 60
aggaactcac tattgaatac ataaatggaa tttattcagc cttaaaaagt ttggaaggaa 120
attctgacat atgctaaaac atggatgaac cttgaagact ttatgataag caaaagaagc 180
cagtcataaa aggaaaaata ttgcatgatt ccacttatat gaggtaccta gugtagtcaa 240
tttcatagaa acacaaaata gaatggtgtt tgccagggct tttgaggaaa agggaatgac 300
aagttagggg acatgagtca gtcta 325

<210> 237
<211> 373
<212> DNA
<213> Homo sapien

<220>
<221> misc feature
<222> (1)..(373)
<223> n = A,T,C or G

<400> 237

tagactgact catgtcccct atctactcaa catttccact tgaagtctga taggcatctc 60
agacttatct tgtcccaaag caaactcttt atttcttttc atcctagtct ttatttcttg 120
tgctgtctta cccatctcaa aagagtgcca aaatccacca agttgctgaa acagaaatct 180
aagaaatatc cttgattctt ctttttccca tctacttcac ttctaattca ttagtaaata 240
atctgtttca gaaaaccaaa cacctcatgt tctcactcat aaggggagt tgaacaatga 300
gaacacacag acacagggag gggaacatca cacaccacgg cccgtcaggg agtangggac 360
atgagtcagt cta 373

<210> 238
<211> 492
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(492)
<223> n = A,T,C or G

<400> 238
tagactgact catgtcccct ataatgctcc caggcatcag aaagcatctc aaactggagc 60
tgacaccatg gcagaggttt caggtaagtc acaaaagggg tcctaaagaa tttgccctca 120
atatcagagt gattagaaga agtggacaga gctacccaag ttaaacatat gcgagataaa 180
aaaaatatgg cacttgtgaa cacacactac aggaggaaaa taaggaacat aatagcatat 240
tgtgctatta tgatgatgaa gaacctctct anaagaaaac ataaccaaag aaacaaagaa 300
aattcctgcn aatgtttaat gctatagaag aaattaacaa aaacatatat tcaatgaatt 360
cagaaaagtt agcaggtcan aagaaaacaa atcaaagacc agaataatcc cattttagat 420
tgtcgagtaa actanaacag aaagaatacc actggaaatt gaattcctac gtangggaca 480
tgantcantc ta 492

<210> 239
<211> 482
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(482)
<223> n = A,T,C or G

<400> 239
tggaaagtat ttaatgatgg gcaacttgct gtttacttcc tacatatccc atcatcttct 60
gtatttttt aaataacttt tttttggatt tttaaagtaa ccttattctg agaggtaaca 120
tggattacat acttctaagc cattaggaga ctctatgtta aaccaaaagg aaatgttact 180
agatcttcat ttgatcaata ggatgtgata atcatcatct ttctgctcta atggaaaagt 240
actanaaaca tggaaccata atcttagatg aacaacgtta gaatttgcac taattctacg 300
gaatttcagt aattcggcaa atgtcgggca gtgacacaac atttcatgac ggggacgcat 360
ctaccaactt ctggcgataa gggccaccct tccctctgca cttacagtcc catttcatac 420
acagtctttg attaaatatt cacatttttt ctctacctaa agaccttcaa gaccagtacg 480
ta 482

<210> 240
<211> 519
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(519)
<223> n = A,T,C or G

<400> 240
tgtatcgacg tagtggtctc cccatgtgat agtctgaaat atagcctcat gggatgagag 60
gctgtgcccc agcccgacac ccgtaaaggg tctgtgctga ggtggattag taaaagagga 120
aagccttgca gttgagatag aggaagggca ctgtctcctg cctgcccctg ggaactgaat 180
gtctcggtat aaaacccgat tgtacatttg ttcaattctg agataggaga aaaaccaccc 240
tatggcggga ggcgagacat gttggcagca atgctgcctt gttatgcttt actccacaga 300
tgtttgggcg gagggaaaca taaatctggc ctacgtgcac atccaggcat agtacctccc 360
tttgaactta attatgacac agattccttt gctcacatgt ttttttgctg accttctcct 420
tattatcacc ctgctctcct accgcattcc ttgtgctgag ataatgaaaa taatatcaat 480
aaaaacttga nggaactcgg agaccactac gtcgatacа 519

<210> 241
<211> 771
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(771)
<223> n = A,T,C or G

<400> 241
tgtatcgacg tagtggtctc cactcccgcc ttgacggggc tgctatctgc cttccaggcc 60
actgtcacgg ctcccgggta gaagtcactt atgagacaca ccagtgtggc cttgttggct 120
tgaagctcct cagaggaggg tgggaacaga gtgaccgagg gggcagcctt gggctgacct 180
aggacggtca gcttggtccc tccgccaaac acgagagtgc tgctgcttgt atatgagctg 240
cagtaataat cagcctcgtc ctcagcctgg agcccagaga tggtcaggga ggccgtgttg 300
ccanacttgg agccagagaa gcgattagaa acccctgagg gccgattacc gacctcataa 360
atcatgaatt tgggggcttt gcctgggtgc tgttggtacc angagacatt attataacca 420
ccaacgtcac tgctggttcc antgcaggga aaatggttga tcnaactgtc caagaaaacc 480
actacgtcca taccaatcca ctaattgccn gccgcctgca ggttcaacca tattggggaa 540
naactccccn ccgccgtttg ggattgncat naacctttga aatttttttcc tattanttgt 600
ccccctaaaa taaaccnttg ggcnttaatc cattgggtcc atancttntt tncccggttt 660
ttaaaanttg tttatcccgc cncccnattt ccccccccaac tttccaaaac ccgaaaccnt 720
tnaaatttnt tnaaaccctg gggggttccc nnaattnnan ttnaanctnc c 771

<210> 242
<211> 167
<212> DNA
<213> Homo sapien

<400> 242
tgggcacctt caatatcggg ctcatcgata acatcacgct gctgatgctg ctgttgctgg 60
tcctctctag gaacctctgg attttcaaat tctttgagga attcatccaa attatctgcc 120
tctcctcctt tcctcctttt tctaaggtct tctggtacaa gcggtca 167

<210> 243
<211> 338
<212> DNA
<213> Homo sapien

<400> 243
ttgggcacct tcaatatcta ctgatctaaa tagtgtggtt tgaggcctct tgttcctggc 60
taaaaatcct tggcaagagt caatctccac tttacaatag aggtaaaaat cttacaatgg 120
atattcttga caaagctagc atagagacag caattttaca caaggtattt ttcacctgtt 180
taataacagt ggttttccta cactcatagg gtgccaccaa gggaggagtg cacagttgca 240
gaaacaaatt aagatactga agacaacact acttaccatt tcccgtatag ctaaccacca 300
gttcaactgt acatgtatgt tcttatgggc aatcaaga 338

<210> 244
<211> 346
<212> DNA
<213> Homo sapien

<400> 244
tttttggctc ccatacagca cactctcatg ggaaatgtct gttctaaggt caacccataa 60
tgcaaaaatc atcaatatac ttgaagatcc ccgtgtaagg tacaatgtat ttaatattat 120
cactgataca attgatccaa taccagtttt agtctggcat tgaatcaaat cactgttttt 180
gttgtataaa aagagaaata tttagcttat atttaagtac catattgtaa gaaaaaagat 240
gcttatcttt acatgctaaa atcatgatct gtacattggt gcagtgaata ttactgtaaa 300
agggaagaag gaatgaagac gagctaagga tattgaaggt gcccaa 346

<210> 245
<211> 521
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(521)
<223> n = A,T,C or G

<400> 245
accaatccca cacggatact gagggacaag tatatcatcc catttcatcc ctacagcagc 60
aacttcatga ggcaggagtt attagtccca ttttacagaa gaggaaactg agacttaggg 120
agatcaagta atttgcccag gtcgcacaat tagtgataga gccagggctt gaagcgacgt 180
ctgtcttaag ccaatgaccc ctgcagatta ttagagcaac tgttctccac aacagtgtaa 240
gcctcttgct anaagctcag gtccacaagg gcagagattt ttgtctgttt tgctcattgc 300
tccttcccca ttgcttagag cagggtctgc cacgaancag gttctcaatg catagttatt 360
aaatgtatat aagagcaaac atatgttaca gagaactttc tgtatgcttg tcacttacat 420
gaatcacctg tganatgggt atgcttgttc cccantgttg cagatnaaga tattgaangt 480
gcccaaatca ctanttgcgg gcgcctgcan gtccancata t 521

<210> 246
<211> 482
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(482)
<223> n = A,T,C or G

<400> 246
tggaaccaat ccaaatаccc atcaatgata gactggataa agaaaatttg gcacatgttc 60

accatgaaat actatgcagc cataaaaaag gatgagttca tatcctttgc agggacatgg 120
atgaagctgg agaccatcat tctcagcaaa ctaacaaggg aacagaaaac caaacactgc 180
atgttctcac tcttaagtgg gagctgaaca atgagaacac atggacacag ggaggggaac 240
atcacacagt ggggcctgct ggtgggtagg ggtctagggg agggatagca ttaggagaaa 300
tacctaatgt agatgacggg ttgatgggtg cagcaaacca ccatgacacg tgtatacctа 360
tgtaacaaac ctgcatgttc tgcacatgta ccccagaact taaagtgtta ataaaaaaat 420
taagaaaaaa gttaagtatg tcatagatac ataaaatatt gtanatattg aaggtgccca 480
aa 482

<210> 247
<211> 474
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(474)
<223> n = A,T,C or G

<400> 247
ttcgatacag gcacagagta agcagaaaaa tggctgtggt ttaacgaagt gagtacagtt 60
aagtgagaga ggggcagaga agacaagggc atatgcaggg ggtgattata acaggtggtt 120
gtgctgggaa gtgagggtac tcggggatga ggaacagtga aaaagtggca aaaagtggta 180
agatcagtga attgtacttc tccagaattt gatttctggn ggagtcaaat aactatccag 240
tttggggtat catanggcaa cagttgaggt ataggaggta gaagtcncag tgggataatt 300
gaggttatga anggtttggt actgactggt actgacaang tctgggttat gaccatggga 360
atgaatgact gtanaagcgt anaggatgaa actattccac ganaaagggg tccnaaaact 420
aaaaannnaa gnnnnnggggg aatattattt atgtggatat tgaangtgcc caaa 474

<210> 248
<211> 355
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(355)
<223> n = A,T,C or G

<400> 248
ttcgatacag gcaaacatga actgcaggag ggtggtgacg atcatgatgt tgccgatggt 60
ccggatggnc acgaagacgc actggancac gtgcttacgt ccttttgctc tgttgatggc 120
cctgagggga cgcaggaccc ttatgaccct cagaatcttc acaacgggag atggcactgg 180
attgantccc antgacacca gagacacccc aaccaccagn atatcantat attgatgtag 240
ttcctgtaga nggccccctt gtggaggaaa gctccatnag ttggtcatct tcaacaggat 300
ctcaacagtt tccgatggct gtgatgggca tagtcatant taaccntgtn tcgaa 355

<210> 249
<211> 434
<212> DNA
<213> Homo sapien

<400> 249
ttggattggt cctccaggag aacaagggga aaaaggtgac cgagggctcc ctggaactca 60
aggatctcca ggagcaaaag gggatggggg aattcctggt cctgctggtc ccttaggtcc 120

acctggtcct ccaggcttac caggtcctca aggcccaaag ggtaacaaag gctctactgg 180
acccgctggc cagaaaggtg acagtggtct tccagggcct cctgggcctc caggtccacc 240
tggtgaagtc attcagcctt taccaatctt gtcctccaaa aaaacgagaa gacatactga 300
aggcatgcaa gcagatgcag atgataatat tcttgattac tcggatggaa tggaagaaat 360
atttggttcc ctcaattccc tgaaacaaga catcgagcat atgaaatttc caatgggtac 420
tcagaccaat ccaa 434

<210> 250
<211> 430
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(430)
<223> n = A,T,C or G

<400> 250
tggattggtc acatggcaga gacaggattc caaggcagtg agaggaggat acaatgcttc 60
tcactagtta ttattattta ttttattttt gagatgaagt ctcgctttgt ctcccaggct 120
ggagagcggt ggtgcgatct tggctctctg caacccccgc ctcaagcaat tctcctgtct 180
tagcctcgcg ggtagatgga attacaggcg cccaccgcca tgcccaacta atttttttgt 240
gtcttcagta gagacagggt ttcgccatgt tgggcaggct ggtcttgaac tcctgacctc 300
nagtgatctg ccctcctcgg cctcacaaag tgctggaatt acaggcatgg gctgctgcac 360
ccagtcaact tctcactagt tatggcctta tcattttcac cacattctat tggcccaaaa 420
aaaaaaaaan 430

<210> 251
<211> 329
<212> DNA
<213> Homo sapien

<400> 251
tggtactcca ccatyatggg gtcaaccgcc atcctcgccc tcctcctggc tgttctccaa 60
ggagtctgtg ccgaggtgca gctgrtgcag tctggagcag aggtgaaaaa gtccggggag 120
tctctgaaga tctcctgtaa gggttctgga tacaccttta gatctactg gatcgcctgg 180
gtgcgccagt tgcccgggaa aggcctggag tggatggggc tcatctttcc tgatgactct 240
gataccagat acagcccgtc cttccaaggc caggtcacca tctcagtcga taagtccatc 300
agcaccgcct atctgcagtg gagtaccaa 329

<210> 252
<211> 536
<212> DNA
<213> Homo sapien

<400> 252
tggtactcca ctcagcccaa ccttaattaa gaattaagag ggaacctatt actattctcc 60
caggctcctc tgctctaacc aggcttctgg gacagtatta gaaaaggatg tctcaacaag 120
tatgtagatc ctgtactggc ctaagaagtt aaactgagaa tagcataaat cagaccaaac 180
ttaatggtcg ttgagacttg tgtcctggag cagctgggat aggaaaactt ttgggcagca 240
agaggaagaa ctgcctggaa gggggcatca tgttaaaaat tacaagggga acccacacca 300
ggcccccttc ccagctctca gcctagagta ttagcatttc tcagctagag actcacaact 360
tccttgctta gaatgtgcca ccgggggggag tccctgtggg tgatgaggct ctcaagagtg 420
agagtggcat cctatcttct gtgtgcccac aggagcctgg cccgagactt agcaggtgaa 480
gttttctggtc caggctttgc ccttgactca ctatgtgacc tctggtggag taccaa 536

<210> 253
<211> 507
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(507)
<223> n = A,T,C or G

<400> 253
ntgttgcgat cccagtaact cgggaagctg aggcgggagg atcacctgag ctcaggaggt 60
tgaggccgca gtgagccggg accacgccac tacactccag cctggggcat agagtgagac 120
cctccaagac agaaaagaaa agaaaggaag ggaaagggaa agggaaaagg aaaaggaaaa 180
ggaaaaggaa aaggaaaaga caagacaaaa caagacttga atttggatct cctgacttca 240
attttatgtt ctttctacac cacaattcct ctgcttacta agatgataat ttagaaaccc 300
ctcgttccat tctttacagc aagctggaag tttggtcaag taattacaat aatagtaaca 360
aatttgaata ttatatgcca ggtgtttttc attcctgctc tcacttaatt ctcaccactc 420
tgatataaat acaattgctg ccgggtgtgg tggctcatgc ctgtaatccc ggcactttgg 480
gagaccgagg tgggcggatc gcaacaa 507

<210> 254
<211> 222
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(222)
<223> n = A,T,C or G

<400> 254
ttggattggt cactgtgagg aagccaaatc ggatccgaga gtcttttttct aaaggccagt 60
actggccaca ctttctcctg ccgccttcct caaagctgaa gacacacaga gcaaggcgct 120
tctgttttac tccccaatgg taactccaaa ccatagatgg ttagctnccc tgctcatctt 180
tccacatccc tgctattcag tatagtccgt ggaccaatcc aa 222

<210> 255
<211> 463
<212> DNA
<213> Homo sapien

<400> 255
tgttgcgatc cataaatgct gaaatggaaa taaacaacat gatgagggag gattaagttg 60
gggagggagc acattaaggt ggccatgaag tttgttggaa gaagtgactt ttgaacaagg 120
ccttggtgtt aagagctgat gagagtgtcc cagacagagg ggccactggt acaatagacg 180
agatgggaga gggcttggaa ggtgtgcgaa ataggaagga gtttgttctg gtatgagtct 240
agtgaacaca gaggcgagag gccctggtgg gtgcagctgg agagttatgc agaataacat 300
taggccctgt gggggactgt agactgtcag caataatcca cagtttggat tttattctaa 360
gagtgatggg aagccgtgga aaggggggtta agcaaggagt gaaattatca gatttacagt 420
gataaaaata aattggtctg gctactgggg aaaaaaaaaa aaa 463

<210> 256
<211> 262

<212> DNA
<213> Homo sapien

<400> 256
ttggattggt caacctgctc aactctacyt ttcctccttc ttcctaaaaa attaatgaat 60
ccaatacatt aatgccaaaa cccttgggtt ttatcaatat ttctgttaaa aagtattatc 120
cagaactgga cataatacta cataataata cataacaacc ccttcatctg gatgcaaaca 180
tctattaata tagcttaaga tcactttcac tttacagaag caacatcctg ttgatgttat 240
tttgatgttt ggaccaatcc aa 262

<210> 257
<211> 461
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(461)
<223> n = A,T,C or G

<400> 257
gnggnnnnnn nnncaattcg actcngttcc cntggtancc ggtcgacatg gccgcgggat 60
taccgcttgt nnctgggggt gtatggggga ctatgaccgc ttgtagctgg gggtgtatgg 120
gggactatga ccgcttgtag mtggkggtgt atgggggact atgaccgctt gtcgggtggt 180
cggataaacc gacgcaaggg acgtgatcga agctgcgttc ccgctctttc gcatcggtag 240
ggatcatgga cagcaatatc cgcattcgyc tgaaggcgtt cgaccatcgc gtgctcgatc 300
aggcgaccgg cgacatcgcc gacaccgcac gccgtaccgg cgcgctcatc cgcggtccga 360
tcccgcttcc cacgcgcatc gagaagttca cggtcaaccg tggcccgcac gtcgacaaga 420
agtcgcgcga gcagttcgag gtgcgtacct acaagcggtc a 461

<210> 258
<211> 332
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(332)
<223> n = A,T,C or G

<400> 258
tgaccgcttg tagctggggg tgtatggggg actacgaccg cttgtagctg ggggtgtatg 60
ggggactatg accgcttgta gctgggggtg tatgggggac tatgaccgct tgtagctggg 120
ggtgtatggg ggactaggac cgcttgtagc tgggggtgta tgggggacta tgaccgcttg 180
tagctggggg tgtatggggg actacgaccg cttgtagctg ggggtgtatg ggggactatg 240
accgcttgta nctgggggtg tatgggggac tatgaccgct tgtgctgcct gggggatggg 300
aggagagttg tggttgggga aaaaaaaaaa aa 332

<210> 259
<211> 291
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature

<222> (1)...(291)
<223> n = A,T,C or G

<400> 259
taccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt 60
gaccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt gaccgcttgt 120
gaccgcttgt gaccgcttgt nacngggggt gtctgggggа ctatgannga ntgtnactgg 180
gggtgtctgg gggnctatga nngantgtna cngggggtgt ctgggggact atganngact 240
gtgcnncctg ggggatcnga ggagantngn ggntagngat ggttngggan a 291

<210> 260
<211> 238
<212> DNA
<213> Homo sapien

<400> 260
taagagggta ctggttaaaa tacaggaaat ctggggtaat gaggcagaga accaggatac 60
tttgaggtca gggatgaaaa ctagaatttt tttctttttt tttgcctgag aaacttgctg 120
ctctgaagag gcccatgtat taattgcttt gatcttcctt ttcttacagc cctttcaagg 180
gcagagccct ccttatcctg aaggaatctt atccttagct atagtatgta ccctctta 238

<210> 261
<211> 746
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(746)
<223> n = A,T,C or G

<400> 261
ttgggcacct tcaatatcaa tagctaacat ttattgagtg tttatcgtat cataaaacac 60
tgttctaagc ctttaaacgt actaattcat ttaatgctca taattacttt agaaggtggg 120
tactagtatt agtctcattt acagatgcaa catgcaggca cagagaggtt aattaacttg 180
cccaaggtaa cacagctaag aaatagaaaa aatattgaat ctggaaagtt gggcttctgg 240
gtaacccaca gagtcttcaa tgagcctggg gcctcactca gtttgctttt acaaagcgaa 300
tgagtaacat cacttaattc agtgagtagg ccaaatggag gtcagctacg agtttctgct 360
gttcttgcag tggactgaca gatgtttaca acgtctggcc atcagtwaat ggactgatta 420
tcattgggaw gtgggtgggc tgaatgttgg ccagtgaagt ttattcawgc catattttta 480
tgtttaggat gacttttggc tggtcctagg gcaagctctg tctgscacgg aacacagaat 540
wacacaggga ccccctcaat ttctggtgtg gctagaacca tgaaccactg gttgggggaa 600
caagcggtca aaacctaagt gcggccggct ggcagggtcc acccatatgg ggaaaactcc 660
cnacgcgttt ggaatgcctn agctngaatt attctaanag ttgtccncnt aaaattagcc 720
tgggcgttaa tcangggtcn naagcc 746

<210> 262
<211> 588
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(588)
<223> n = A,T,C or G

<400> 262
tgaccgcttg tcatctcaca tggggtcctg cacgcttttg cctttgtagg aaacctgaca 60
tttgtctgtt tcttctttct cttttccttc ccatatcctc ctaatttacg tttgacttgt 120
ttgctgagga ggcaggagct agagactgct gtgagctcat aggggtggga agtttatcct 180
tcaagtcccg cccactcatc actgcttctc accttccccc gaccaggctt acaagtgggt 240
tcttgcctgc tttccctttg gacccaacaa gcccctgtaa tgagtgtgca tgactctgac 300
agctgtggac tcagggtcct tggctacagc tgccatgtaa aatatctcat ccagttctcg 360
caaattgtta aaataaccac atttcttaga ttccagtacc caaatcatgt ctttacgaac 420
tgctcctcac acccagaagt ggcacaataa ttcttgggga attattactt ttttttttct 480
ctctnttnnc gnnngnnnng gnnngnccag gaattaccac nttggaagac ctggccngaa 540
tttattatan aggggagccg attnttttte ctaacacaaa gcgggtca 588

<210> 263
<211> 730
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(730)
<223> n = A,T,C or G

<400> 263
ttttttttnt tttggcctga gcaactgaaa ttatgaaatt tccatatact caaaagagta 60
agactgcaaa aagattaaat gtaaaagttg tcttgtatac agtaatgttt aagataccta 120
ttanatttat aaatggaaaa ttagggcatt tggatataca agttgaaaat tcaggagtga 180
ggttgggctg gctgggtata tactgaaaac tgtcagtaca cagatgacat ctaaaaccac 240
aaatctggtt ttattttagc agtgatatgt gtcactccca caaaagcctt cccaattggc 300
ctcagcatac acaacaagtc acctccccac agccctctac acataaacaa attccttagt 360
ttagttcagg aggaaatgcg ccctttttcct tccgctctag gtgaccgcaa ggcccagttc 420
tcgtcaccaa gatgttaagg gaagtctgcc aaagaggcat ctgaaaggaa ataaggggaa 480
tgggagtgac cacaaaggaa agccaaggan aaactttgga gaccgtttct agancctgg 540
catttcacaa caaaactcng gaacaaacct tgtctcatca atcatttaag cccttcgttt 600
ggannagact ttctgaactg ggcgctgaac ataancctca ttgaatgtct tcacagtctc 660
ccagctgaag gcacaccttg ggccagaagg ggaatcttcc aggtcctcaa nacagggctc 720
gccctttgnc 730

<210> 264
<211> 715
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(715)
<223> n = A,T,C or G

<400> 264
ttttttttnt tttggccagt atgatagtct ctaccactat attgaagctc ttaggtcatt 60
tacacttaat gtggttatag atgctgttga gcttacttct accaccttgc tatttctccc 120
gtctcttttt tgttcctttt ctcttctttt cctcccttat tttataattg aatttttttag 180
gattctattt tatatagatt tatcagctat aacactttgt attcttttgt tttgtggttc 240
ttctgtcatt tcaatgtgca tcttaaactc atcacaatct attttcaaat aatatcatat 300
aaccttacat ataatgtaag aatctaccac catatatttc catttctccc ttccatccta 360

tgtntgtcat attttttcct ttatatatgt tttaaagaca taatagtata tgggaggttt 420
ttgcttaaaa tgtgatcaat attccttcaa ngaaacgtaa aaattcaaaa taaatntctg 480
tttattctca aatnnaccta atatttccta ccatntctna tacntttcaa gaatctgaag 540
gcattggttt tttccggctt aagaacctcc tctaaagcac tctaagcaga attaagtctt 600
ctgggagagg aattctccca agcttgggcc ttnanntgta ctccntnang gttaaanttt 660
ggccgggaaa tagaaattcc aagttaacag gntantttttt nttttttnttn tcncc 715

<210> 265
<211> 152
<212> DNA
<213> Homo sapien

<400> 265
ttttttttttt tttcccaaca caaagcacca ttatctttcc tcacaatttt caacatagtt 60
tgattcccat gaagaggtta tgatttctaa agaaaacatg gctactatac tatcaatcag 120
ggttaaatct ttttttttttg agacggagtt ta 152

<210> 266
<211> 193
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(193)
<223> n = A,T,C or G

<400> 266
taaactccgt ccccttctta atcaatatgg aggctaccca ctccacatta cctttttttc 60
aagggactgt ttccgtaact gttgtgggta ttcacgacca ggcttctaaa cctcttaaaa 120
ctccccaatt ctggtgccaa cttggacaac atgctttttt ttttttttttt ttttttttnn 180
gagacggagt tta 193

<210> 267
<211> 460
<212> DNA
<213> Homo sapien

<400> 267
tgttgcgatc ccttaagcat gggtgctatt aaaaaaatgg tggagaagaa aatacctgga 60
atttacgtct tatctttaga gattgggaag accctgatgg aggacgtgga gaacagcttc 120
ttcttgaatg tcaattccca agtaacaaca gtgtgtcagg cacttgctaa ggatcctaaa 180
ttgcagcaag gctacaatgc tatgggattc tcccagggag gccaatttct gagggcagtg 240
gctcagagat gcccttcacc tcccatgatc aatctgatct cggttggggg acaacatcaa 300
ggtgtttttg gactccctcg atgcccagga gagagctctc acatctgtga cttcatccga 360
aaaacactga atgctggggc gtactccaaa gttgttcagg aacgcctcgt gcaagccgaa 420
tactggcatg acccataaaa ggaggatgtg gatcgcaaca 460

<210> 268
<211> 533
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature

<222> (1)...(533)
<223> n = A,T,C or G

<400> 268
tgttgcgatc cgttgataga atagcgacgt ggtaatgagt gcatggcacg cctccgactt 60
accttcgccc gtggggaccc cgagtacgtc tacggcgtcg tcacttagag taccctctgg 120
acgcccgggc gcgttcgatt taccggaagc gcgagctgca gtgggcttgc gccccggcc 180
aaattctttg gggggtttaa ggccgcgggg aatttgaggt atctctatca gtatgtagcc 240
aagttggaac agtcgccatt cccgaaatcg ctttctttga atccgcaccg cctccagcat 300
tgcctcattc atcaacctga aggcacgcat aagtgacggt tgtgtcttca gcagctccac 360
tccataacta gcgcgctcga cctcgtcttc gtacgcgcca ggtccgtgcg tgcgaattcc 420
caactccggt gagttgcgca tttcaagttn cgaaactgtt cgcctccacn atttggcatg 480
ttcacgcatg acacggaata aactcgtcca gtaccgggaa tgggatcgca aca 533

<210> 269
<211> 50
<212> DNA
<213> Homo sapien

<400> 269
ttttttttt ttcgcctgaa ttagctacag atcctcctca caagcggtca 50

<210> 270
<211> 519
<212> DNA
<213> Homo sapien

<400> 270
tgttgcgatc caaataaccc accagcttct tgcacacttc gcagaagcca ccgtcctttg 60
gctgagtcac gtgaacggtc agtgcaagca gccgcgtgcc agagcagagg tgcagcatgc 120
tgcacaccag ctcagggctg acctcctcca gcaggatgga caggatggag ctgccgtacg 180
tgtccaccac ctcctggcac tcttccgaca gggacttcgg cagcttcgag cacattttgt 240
caaaagcgtc gagtatttct ttctcagtct tgttgttgtc aatcagcttg gtcacctcct 300
tcaccaggaa ttcacacacc tcacagtaaa catcagactt tgctgggacc tcgtgcttct 360
taatgggctc caccagttcc agggcaggga tgacattctt ggaggccact ttggcgggga 420
ccagagtctg catgggcatc tctttcacct catcacagaa cccaaccagc gcacagatct 480
ccttgggttg catgtgcatc atcatctggg atcgcaaca 519

<210> 271
<211> 457
<212> DNA
<213> Homo sapien

<400> 271
ttttttttt ttcgggcggc gaccggacgt gcactcctcc agtagcggct gcacgtcgtg 60
ccaatggccc gctatgagga ggtgagcgtg tccggcttcg aggagttcca ccgggccgtg 120
gaacagcaca atggcaagac cattttcgcc tactttacgg gttctaagga cgccgggggg 180
aaaagctggt gccccgactg cgtgcaggct gaaccagtcg tacgagaggg gctgaagcac 240
attagtgaag gatgtgtgtt catctactgc caagtaggag aagagcctta ttggaaagat 300
ccaaataatg acttcagaaa aaacttgaaa gtaacagcag tgcctacact acttaagtat 360
ggaacacctc aaaaactggt agaatctgag tgtcttcagg ccaacctggt ggaaatgttg 420
ttctctgaag attaagattt taggatggca atcaaga 457

<210> 272
<211> 102

<212> DNA
<213> Homo sapien

<400> 272
ttttttttttttgggcaaca acctgaatac cttttcaagg ctctggcttg ggctcaagcc 60
cgcaggggaa atgcaactgg ccaggtcaca gggcaatcaa ga 102

<210> 273
<211> 455
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(455)
<223> n = A,T,C or G

<400> 273
ttttttttttttggcaatca acaggtttaa gtcttcggcc gaagttaatc tcgtgttttt 60
ggcaatcaac aggtttaagt cttcggccga agttaatctc gtgtttttgg caatcaacag 120
gtttaagtct tcggccgaag ttaatctcgt gtttttggca atcaacaggt ttaagtcttc 180
ggccgaagtt aatctcgtgt ttttggcaat caacaggttt aagtcttcgg ccgaagttaa 240
tctcgtgttt ttggcaatca acaggtttaa gtcttcggcc gaagttaatc tcgtgttttt 300
ggcaatcaag aggtttaagt cttcggccga agttaatctc gtgtttttgg caatcaacag 360
gtttaagtct tcggccgaan ttaatctcgt gtttttggca atcaacaggt ttaantcttc 420
ggccgaagtt aatctcgtgt ttttggcaat caana 455

<210> 274
<211> 461
<212> DNA
<213> Homo sapien
<400> 274
ttttttttttttggccaata cccttgatga acatcaatgt gaaaatcctc ggtaaaatac 60
tggcaaacca aatccagcag cacatcaaaa agcttatcca ccatgatcaa gtgggcttca 120
tccctgggat gcaaggctgg ttcaacataa gaaaatcaat aaatgtaatc catcacataa 180
acagaaccaa agacaaaaac cacatgatta tctcaataga tgcagaaaag gccttggaca 240
aattcaacag cccttcatgc taaacactct taataaacta gatattgatg gaatgtatct 300
caaaataata agagctattt atgacaaacc cacagccaat atcatactga atgggcaaag 360
actggaagca ttccctttga aaactggcac aagacaagga tgccctctct caccgctcct 420
attcaacata gtattggaag ttctggccag ggcaatcaag a 461

<210> 275
<211> 729
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)...(729)
<223> n = A,T,C or G

<400> 275
ttttttttttttggccaaca ccaagtcttc cacgtgggag gttttattat gttttacaac 60
catgaaaaca taggaaggtg gctgttacag caaacatttc agatagacga atcggccaag 120

ctccccaaac cccaccttca cagcctcttc cacacgtctc ccanagattg ttgtccttca 180
cttgcaaatt canggatgtt ggaagtngac atttnnagtn gcnggaaccc catcagtgaa 240
ncantaagca gaantacgat gactttgana nacanctgat gaagaacacn ctacnganaa 300
ccctttctnt cgtgttanga tctcnngtcc ntcactaatg cggccccctg cnggtccacc 360
atttgggaga actccccccn cgttggatcc ccccttgagt ntcccattct ngtccccccan 420
accngncttg ngngncantn cnncctcnca ccntgtttcc ctgnngtnaa aatnngtttt 480
nccgccnccc naattcccac ccnaatcaca gcgaanccng aaggccttcn naagtgttta 540
angcccngng gtttcctcnt ntanttgcag cctaccctcc cnctttnnnnt tncgngttgg 600
tcgcgccctg gncncgcctn gttcctcttt nnggnnacaa cctngntcnn nggcncntcn 660
nnnctnttcc tnnnactagc tngcctntcc ncnccgnggn ncanngcaca ttncncnnac 720
tntgtnncc 729

<210> 276
<211> 339
<212> DNA
<213> Homo sapien

<400> 276
tgacctgaca tgtagtagat acttaataaa tatttgtgga atgaatggat gaagtggagt 60
tacagagaaa aatagaaaag tacaaattgt tgtcagtgtt ttgaaggaaa attatgatct 120
ttcccaaagt totgacttca ttctaagaca gggttagtat ctccatacat aattttactt 180
gcttttgaaa atcaaatgag ataatctatt tagattgata atttatttag actggctata 240
aactattaag tgctagcaa tatacatttt aatctcattt tccacctctt gtgatatagc 300
tatgtaggtg ttgactttaa tggatgtcag gtcaatccc 339

<210> 277
<211> 664
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(664)
<223> n = A,T,C or G

<400> 277
tgacctgaca tccataacaa aatctttctc cattatattc ttctagggga atttcttgaa 60
aagcatccaa aggaaacaaa tgatggtaag accgtgccaa gtggggagca gacaccaaag 120
taagaccaca gattttacat tcaacaggta gctcacagta ctttgcccga cactgtgggc 180
agaaatagcc tcctaatgta agccctggct cagtattgcc atccaaatgc gccatgctga 240
aagagggttt tgcatcctgg tcagatnaag aagcaatggt gtgctgagga aatcccatac 300
gaataagtga gcattcagaa cttgagctag caggaggagg actaagatga tgtgtgagca 360
actctttgta atggctttca tctaaaataa catggtacgt gccaccagtt tcacgagcaa 420
gtacagtgca aacgcgaact tctgcagaca atccaataac agatactcta attttagctg 480
cctttagggt cttgattaaa tcataaatat tagatggatc gcaagttgta aggntgctaa 540
aagatgatta gtacttctcg acttgtatgt ccaggcatgt tgttttaaan tctgccttag 600
nccctgctta ggggaatttt taaagaagat ggctctccat gttcanggtc aatcacnaat 660
tgcc 664

<210> 278
<211> 452
<212> DNA
<213> Homo sapien
<220>

<221> misc_feature
<222> (1)..(452)
<223> n = A,T,C or G

<400> 278
tgacctgaca ttgaggaaga gcacacacct ctgaaattcc ttaggttcag aagggcattt 60
gacacagagt gggcctctga taattcatga aatgcattct gaagtcatcc agaatggagg 120
ctgcaatctg ctgtgctttg ggggttgcct cactgtgctc ctggatatca cacaaaagct 180
gcaatccttc ttcttcaact aacattttgc agtatttgct gggatttta ctgcagacat 240
gatacatagc ccatagtgcc cagagctgaa cctctggttg agagaagttg ccaaggagcg 300
ggaaaaatgt cttgaaagat ctataggtca ccaatgctgt catcttacaa cttgaacttg 360
gccaattctg tatggttgca tgcagatctt ggagaagagt acgcctctgg aagtcacggg 420
atatccaaan ctgtctgtca gatgtcaggt ca 452

<210> 279
<211> 274
<212> DNA
<213> Homo sapien

<400> 279
ttttttttt ttcggcaagg caaatttact tctgcaaaag ggtgctgctt gcacttttgg 60
ccactgcgag agcacaccaa acaaagtagg gaaggggttt ttatccctaa cgcggttatt 120
ccctggttct gtgtcgtgtc cccattggct ggagtcagac tgcacaatct acactgaccc 180
aactggctac tgtttaaaat tgaatatgaa taattaggta ggaaggggga ggctgtttgt 240
tacggtacaa gacgtgtttg ggcatgtcag gtca 274

<210> 280
<211> 272
<212> DNA
<213> Homo sapien

<400> 280
tacctgacat ggagaaataa cttgtagtat tttgcgtgca atggaatact atatgagggt 60
gaaaatgaat gaactagcaa tgcgtgtatc aacatgaata aatccccaaa acataataat 120
gttgaatgga aaaggtgagt ttcagaagga tatatatgcc ctctaaatcc atttatgtaa 180
acctttaaaa aactacatta tttatggtca taagtccatc cagaaaatat ttaaaaacct 240
acatgggatt gataactact gatgtcaggt ca 272

<210> 281
<211> 431
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)..(431)
<223> n = A,T,C or G

<400> 281
ttttttttt ttggccaata gcatgattta aacattggaa aaagtcaaat gagcaatgcg 60
aatttttatg ttctcttgaa taatcaaaag agtaggcaac attggttcct cattcttgaa 120
tagcattaat cagaaaatat tgcatagcct ctagcctcct tagagtaggt gtgctctctc 180
aaatatatca tagtcccaca gtttatttca tgtatatttt ctgcctgaat cacatagaca 240
tttgaatttg caacgcctga tgtaaatata taaattctta ccaatcagaa acatagcaag 300
aaattcaggg acttggtcat yatcagggta tgacagcana tccctgtara aacactgata 360

cacactcaca cacgtatgca acgtggagat gtcgcyttww kkktwywcwm rmrycrwcgn 420
aatcacttan n 431

<210> 282
<211> 98
<212> DNA
<213> Homo sapien

<400> 282
attcgattcg atgcttgagc ccaggagttc aagactgcag tgagccactg cacttcaggc 60
tggacaacag agcgagtccc tgtgccaaaa aaaaaaaa 98

<210> 283
<211> 764
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(764)
<223> n = A,T,C or G

<400> 283
ttttttttt ttcgcaagca cgtgcacttt attgaatgac actgtagaca ggtgtgtggg 60
tataaactgc tgtatctagg ggcaggacca agggggcagg ggcaacagcc ccagcgtgca 120
gggccascat tgcacagtgg astgcaaagg ttgcaggcta tgggcggcta ctavtaaccc 180
cgtttttcct gtattatctg taacataata tggtagactg tcacagagcc gaatwccart 240
hacasgatga atccaawggt caygaggatg cccasaatca gggcccasat sttcaggcac 300
ttggcggtgg gggcatasgc ctgkgccccg gtcacgtcsc caaccwtcty cctgtcccta 360
cmcttgawtc cncncccttnn nntnccntna tntgcccgcc cncctcctng ngtcaaccng 420
natctgcact anctcccten ccccttntgg antctcntcc ttcaantaan nttatccttn 480
acncccccct cncctttccc ctnccncccn tnatcccngn nccnctatca ntcntnccct 540
cnctntnctn cnnatcgttc cncctnntaa ctacnctttn nacnanncct cactnatncc 600
ngnnanttct ttccttcccc cccnacgcnn tgcgtgcgcc cgtctnccct nnnctncgna 660
cccnnacttt atttaccttt ncaccctagc nctctacttn acccanccnc tcctacctcc 720
nggnccaccc nnccctnatc nctnnctctn tcnnctcntt cccc 764

<210> 284
<211> 157
<212> DNA
<213> Homo sapien

<400> 284
caagtgtagg cacagtgatg aaagcctgga gcaaacacaa tctgtgggta attaacgttt 60
atttctcccc ttccaggaac gtcttgcatg gatgatcaaa gatcagctcc tggtcaacat 120
aaataagcta gtttaagata cgttccccta cacttga 157

<210> 285
<211> 150
<212> DNA
<213> Homo sapien

<400> 285
attcgattgt actcagacaa caatatgcta agtggaagaa gtcagtcaca aaagaccaca 60
tactgtatga cttcatttac attaagtgtc cagaataggc aaatccgtag agacagaaag 120

tagatgagca gctgcctagg tctgagtaca 150

<210> 286
<211> 219
<212> DNA
<213> Homo sapien

<400> 286
attcgatttt ttttttttg gccatgatga aattcttact ccctcagatt ttttgtctgg 60
ataaatgcaa gtctcaccac cagatgtgaa attacagtaa actttgaagg aatctcctga 120
gcaaccttgg ttaggatcaa tccaatattc accatctggg aagtcaggat ggctgagttg 180
caggtcttta caagttcggg ctggattggt ctgagtaca 219

<210> 287
<211> 196
<212> DNA
<213> Homo sapien

<400> 287
attcgattct tgaggctacc aggagctagg agaagaggca tggaacaaat tttccctcat 60
atccatactc agaaggaacc aaccctgctg acaccttaat ttcagcttct ggcctctaga 120
actgtgagag agtacatttc tcttggttta agccaagaga atctgtcttt tggtacttta 180
tatcatagcc tcaaga 196

<210> 288
<211> 199
<212> DNA
<213> Homo sapien

<400> 288
attcgatttc agtccagtcc cagaacccac attgtcaatt actactctgt araagattca 60
tttgttgaaa ttcattgagt aaaacattta tgatccctta atatatgcca attaccatgc 120
taggtactga agattcaagt gaccgagatg ctagcccttg ggttcaagtg atccctctcc 180
cagagtgcac tggactgaa 199

<210> 289
<211> 182
<212> DNA
<213> Homo sapien

<400> 289
attcgattct tgaggctaca aacctgtaca gtatgttact ctactgaata ctgtaggcaa 60
tagtaataca gaagcaagta tctgtatatg taaacattaa aaaggtacag tgaaacttca 120
gtattataat cttagggacc accattatat atgtggtcca tcattggcca aaaaaaaaaa 180
aa 182

<210> 290
<211> 1646
<212> DNA
<213> Homo sapien

<400> 290
ggcacgagga gaaatgtaat tccatatttt atttgaaact tattccatat tttaattgga 60
tattgagtga ttgggttatc aaacacccac aaactttaat tttgttaaat ttatatggct 120
ttgaaataga agtataagtt gctaccattt tttgataaca ttgaaagata gtatttttacc 180

atctttaatc atcttggaaa atacaagtcc tgtgaacaac cactctttca cctagcagca 240
tgaggccaaa agtaaaggct ttaaattata acatatggga ttcttagtag tatgtttttt 300
tcttgaaact cagtggctct atctaacctt actatctcct cactctttct ctaagactaa 360
actctaggct cttaaaaatc tgcccacacc aatcttagaa gctctgaaaa gaatttgtct 420
ttaaatatct tttaatagta acatgtattt tatggaccaa attgacattt tcgactattt 480
tttccaaaaa agtcaggtga atttcagcac actgagttgg gaatttctta tcccagaaga 540
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gcagtctcct taaaggtaga acaaatactt tctatttttt tttcaccatt gtgggattgg 660
actttaagag gtgactctaa aaaaacagag aacaaatatg tctcagttgt attaagcacg 720
gacccatatt atcatattca cttaaaaaaa tgatttcctg tgcacctttt ggcaacttct 780
cttttcaatg tagggaaaaa cttagtcacc ctgaaaaccc acaaaataaa taaaacttgt 840
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gagcagaagc aaaccacatg tctcagctat attattattt atttttatg cataaagtga 1020
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cagtgcattg acaatgggtt gatatttttc tttaaaagaa aaatataatt atgaaagcca 1140
agataatctg aagcctgttt tattttaaaa ctttttatgt tctgtggttg atgttgtttg 1200
tttgtttgtt tctatttttgt tggtttttta ctttgttttt tgttttgttt tgttttgttt 1260
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ctggtaattt ttttatttac aatatgttta aagagataac agtttgatat gttttcatgt 1440
gtttatagca gaagttattt atttctatgg cattccagcg gatattttgg tgtttgcgag 1500
gcatgcagtc aatattttgt acagttactg gacagtattc agcaacgcct gatagcttct 1560
ttggccttat gttaaataaa aagacctgtt tgggatgtat tttttatttt taaaaaaaaa 1620
aaaaaaaaaa aaaaaaaaaa aaaaaa 1646

<210> 291
<211> 1851
<212> DNA
<213> Homo sapien

<400> 291
tcatcaccat tgccagcagc ggcaccgtta gtcaggtttt ctgggaatcc cacatgagta 60
cttccgtgtt cttcattctt cttcaatagc cataaatctt ctagctctgg ctggctgttt 120
tcacttcctt taagcctttg tgactcttcc tctgatgtca gctttaagtc ttgttctgga 180
ttgctgtttt cagaagagat ttttaacatc tgtttttctt tgtagtcaga aagtaactgg 240
caaattacat gatgatgact agaaacagca tactctctgg ccgtctttcc agatcttgag 300
aagatacatc aacattttgc tcaagtagag ggctgactat acttgctgat ccacaacata 360
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<210> 292
<211> 1851
<212> DNA
<213> Homo sapien

<400> 292
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cagcaagtat gagagcagtt cttccatatc tatccagcgc atttaaattc gcttttttct 420
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<211> 668
<212> DNA
<213> Homo sapien

<400> 293
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accrtataag agcagtgctt tggccattaa tttatctttc attrtagaca gcrtagtgya 180
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cgtctgtcca gcaggagttt tactacttct gaattcccat tggcagaggc cagatgtaga 540
gcagtcctat gagagtgaga agacttttta ggaaattgta gtgcactagc tacagccata 600
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aaaaaaaa 668

<210> 294
<211> 1512
<212> DNA
<213> Homo sapien

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<210> 295
<211> 1853
<212> DNA
<213> Homo sapien

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<210> 296
<211> 2184
<212> DNA
<213> Homo sapien

<400> 296
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<210> 297
<211> 1855
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1)..(1855)
<223> n = A,T,C or G

<400> 297
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<210> 298
<211> 1059
<212> DNA
<213> Homo sapien

<400> 298
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<210> 299
<211> 329
<212> PRT
<213> Homo sapien

<400> 299
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Leu His Leu Ala Gly Ser Asp Leu Leu Ser Arg Ser Leu Met Ala Glu
20 25 30
Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser
35 40 45
Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg
50 55 60
Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val
65 70 75 80
Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val
85 90 95
Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
100 105 110
His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
115 120 125
Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
130 135 140
Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser

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145                 150                 155                 160
Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys
                165                 170                 175
Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
            180                 185                 190
Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
        195                 200                 205
Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
    210                 215                 220
Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
225                 230                 235                 240
Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
                245                 250                 255
Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
            260                 265                 270
Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
        275                 280                 285
Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu
    290                 295                 300
Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu
305                 310                 315                 320
Ser Met Leu Phe Leu Val Ile Ile Met
                325
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<210> 300
<211> 148
<212> PRT
<213> Homo sapien

<220>
<221> VARIANT
<222> (1)...(148)
<223> Xaa = Any Amino Acid

<400> 300

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Met Thr Xaa Pro Ser Trp Ser Pro Gly Thr Thr Ser Val Glu Lys Ile
 1                5                  10                  15
Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys
            20                  25                  30
Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys
        35                  40                  45
Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu
    50                  55                  60
Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp
65                  70                  75                  80
Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp
                85                  90                  95
Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro
            100                 105                 110
Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp
        115                 120                 125
Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser
    130                 135                 140
Lys Asn Lys Val
145
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<210> 301
<211> 1155
<212> DNA
<213> Homo sapien

<400> 301
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agcaacgtgg gcacttctgg agaccacgac gactctgcta tgaagacact caggagcaag 180
atgggcaagt ggtgccgcca ctgcttcccc tgctgcaggg ggagtggcaa gagcaacgtg 240
ggcgcttctg gagaccacga cgactctgct atgaagacac tcaggaacaa gatgggcaag 300
tggtgctgcc actgcttccc ctgctgcagg gggagcggca agagcaaggt gggcgcttgg 360
ggagactacg atgacagtgc cttcatggag cccaggtacc acgtccgtgg agaagatctg 420
gacaagctcc acagagctgc ctggtggggt aaagtcccca gaaaggatct catcgtcatg 480
ctcagggaca ctgacgtgaa caagaaggac aagcaaaaga ggactgctct acatctggcc 540
tctgccaatg ggaattcaga agtagtaaaa ctcctgctgg acagacgatg tcaacttaat 600
gtccttgaca acaaaaagag gacagctctg ataaaggccg tacaatgcca ggaagatgaa 660
tgtgcgttaa tgttgctgga acatggcact gatccaaata ttccagatga gtatggaaat 720
accactctgc actacgctat ctataatgaa gataaattaa tggccaaagc actgctctta 780
tatggtgctg atatcgaatc aaaaaacaag catggcctca caccactgtt acttggtgta 840
catgagcaaa aacagcaagt cgtgaaattt ttaatcaaga aaaaagcgaa tttaaatgca 900
ctggatagat atggaaggac tgctctcata cttgctgtat gttgtggatc agcaagtata 960
gtcagccttc tacttgagca aaatattgat gtatcttctc aagatctatc tggacagacg 1020
gccagagagt atgctgtttc tagtcatcat catgtaattt gccagttact ttctgactac 1080
aaagaaaaac agatgctaaa aatctcttct gaaaacagca atccagaaaa tgtctcaaga 1140
accagaaata aataa 1155

<210> 302
<211> 2000
<212> DNA
<213> Homo sapien

<400> 302
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agcaacgtgg gcacttctgg agaccacgac gactctgcta tgaagacact caggagcaag 180
atgggcaagt ggtgccgcca ctgcttcccc tgctgcaggg ggagtggcaa gagcaacgtg 240
ggcgcttctg gagaccacga cgactctgct atgaagacac tcaggaacaa gatgggcaag 300
tggtgctgcc actgcttccc ctgctgcagg gggagcggca agagcaaggt gggcgcttgg 360
ggagactacg atgacagtgc cttcatggag cccaggtacc acgtccgtgg agaagatctg 420
gacaagctcc acagagctgc ctggtggggt aaagtcccca gaaaggatct catcgtcatg 480
ctcagggaca ctgacgtgaa caagaaggac aagcaaaaga ggactgctct acatctggcc 540
tctgccaatg ggaattcaga agtagtaaaa ctcctgctgg acagacgatg tcaacttaat 600
gtccttgaca acaaaaagag gacagctctg ataaaggccg tacaatgcca ggaagatgaa 660
tgtgcgttaa tgttgctgga acatggcact gatccaaata ttccagatga gtatggaaat 720
accactctgc actacgctat ctataatgaa gataaattaa tggccaaagc actgctctta 780
tatggtgctg atatcgaatc aaaaaacaag catggcctca caccactgtt acttggtgta 840
catgagcaaa aacagcaagt cgtgaaattt ttaatcaaga aaaaagcgaa tttaaatgca 900
ctggatagat atggaaggac tgctctcata cttgctgtat gttgtggatc agcaagtata 960
gtcagccttc tacttgagca aaatattgat gtatcttctc aagatctatc tggacagacg 1020
gccagagagt atgctgtttc tagtcatcat catgtaattt gccagttact ttctgactac 1080
aaagaaaaac agatgctaaa aatctcttct gaaaacagca atccagaaca agacttaaag 1140
ctgacatcag aggaagagtc acaaaggttc aaaggcagtg aaaatagcca gccagagaaa 1200
atgtctcaag aaccagaaat aaataaggat ggtgatagag aggttgaaga agaaatgaag 1260

aagcatgaaa gtaataatgt gggattacta gaaaacctga ctaatggtgt cactgctggc 1320
aatggtgata atggattaat tcctcaaagg aagagcagaa cacctgaaaa tcagcaattt 1380
cctgacaacg aaagtgaaga gtatcacaga atttgcgaat tagtttctga ctacaaagaa 1440
aaacagatgc caaaatactc ttctgaaaac agcaacccag aacaagactt aaagctgaca 1500
tcagaggaag agtcacaaag gcttgagggc agtgaaaatg gccagccaga gctagaaaat 1560
tttatggcta tcgaagaaat gaagaagcac ggaagtactc atgtcggatt cccagaaaac 1620
ctgactaatg gtgccactgc tggcaatggt gatgatggat taattcctcc aaggaagagc 1680
agaacacctg aaagccagca atttcctgac actgagaatg aagagtatca cagtgacgaa 1740
caaaatgata ctcagaagca attttgtgaa gaacagaaca ctggaatatt acacgatgag 1800
attctgattc atgaagaaaa gcagatagaa gtggttgaaa aaatgaattc tgagctttct 1860
cttagttgta agaaagaaaa agacatcttg catgaaaata gtacgttgcg ggaagaaatt 1920
gccatgctaa gactggagct agacacaatg aaacatcaga gccagctaaa aaaaaaaaaa 1980
aaaaaaaaaa aaaaaaaaaa 2000

<210> 303
<211> 2040
<212> DNA
<213> Homo sapien

<400> 303
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aggagcaaga tgggcaagtg gtgctgccgt tgcttccgct gctgcaggga gagcggcaag 120
agcaacgtgg gcacttctgg agaccacgac gactctgcta tgaagacact caggagcaag 180
atgggcaagt ggtgccgcca ctgcttcccc tgctgcaggg ggagtggcaa gagcaacgtg 240
ggcgcttctg gagaccacga cgactctgct atgaagacac tcaggaacaa gatgggcaag 300
tggtgctgcc actgcttccc ctgctgcagg gggagcggca agagcaaggt gggcgcttgg 360
ggagactacg atgacagtgc cttcatggag cccaggtacc acgtccgtgg agaagatctg 420
gacaagctcc acagagctgc ctggtggggt aaagtcccca gaaaggatct catcgtcatg 480
ctcagggaca ctgacgtgaa caagaaggac aagcaaaaga ggactgctct acatctggcc 540
tctgccaatg ggaattcaga agtagtaaaa ctcctgctgg acagacgatg tcaacttaat 600
gtccttgaca acaaaaagag gacagctctg ataaaggccg tacaatgcca ggaagatgaa 660
tgtgcgttaa tgttgctgga acatggcact gatccaaata ttccagatga gtatggaaat 720
accactctgc actacgctat ctataatgaa gatatattaa tggccaaagc actgctctta 780
tatggtgctg atatcgaatc aaaaaacaag catggcctca caccactgtt acttggtgta 840
catgagcaaa aacagcaagt cgtgaaattt ttaatcaaga aaaaagcgaa tttaaatgca 900
ctggatagat atggaaggac tgctctcata cttgctgtat gttgtggatc agcaagtata 960
gtcagccttc tacttgagca aaatattgat gtatcttctc aagatctatc tggacagacg 1020
gccagagagt atgctgtttc tagtcatcat catgtaattt gccagttact ttctgactac 1080
aaagaaaaac agatgctaaa aatctcttct gaaaacagca atccagaaca agacttaaag 1140
ctgacatcag aggaagagtc acaaaggttc aaaggcagtg aaaatagcca gccagagaaa 1200
atgtctcaag aaccagaaat aaataaggat ggtgatagag aggttgaaga agaaatgaag 1260
aagcatgaaa gtaataatgt gggattacta gaaaacctga ctaatggtgt cactgctggc 1320
aatggtgata atggattaat tcctcaaagg aagagcagaa cacctgaaaa tcagcaattt 1380
cctgacaacg aaagtgaaga gtatcacaga atttgcgaat tagtttctga ctacaaagaa 1440
aaacagatgc caaaatactc ttctgaaaac agcaacccag aacaagactt aaagctgaca 1500
tcagaggaag agtcacaaag gcttgagggc agtgaaaatg gccagccaga gaaaagatct 1560
caagaaccag aaataaataa ggatggtgat agagagctag aaaatttttat ggctatcgaa 1620
gaaatgaaga agcacggaag tactcatgtc ggattcccag aaaacctgac taatggtgcc 1680
actgctggca atggtgatga tggattaatt cctccaagga agagcagaac acctgaaagc 1740
cagcaatttc ctgacactga gaatgaagag tatcacagtg acgaacaaaa tgatactcag 1800
aagcaatttt gtgaagaaca gaacactgga atattacacg atgagattct gattcatgaa 1860
gaaaagcaga tagaagtggt tgaaaaaatg aattctgagc ttctcttag ttgtaagaaa 1920
gaaaaagaca tcttgcatga aaatagtacg ttgcgggaag aaattgccat gctaagactg 1980
gagctagaca caatgaaaca tcagagccag ctaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2040

<210> 304
<211> 384
<212> PRT
<213> Homo sapien

<400> 304

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
1 5 10 15

Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
20 25 30

Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
35 40 45

His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
50 55 60

Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
65 70 75 80

Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
85 90 95

Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
100 105 110

Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
115 120 125

Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
130 135 140

Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
145 150 155 160

Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
165 170 175

Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
180 185 190

Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
195 200 205

Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
210 215 220

Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
225 230 235 240

Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
245 250 255

Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
260 265 270

Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
275 280 285

Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
290 295 300

Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
305 310 315 320

Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
325 330 335

Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
340 345 350

Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
355 360 365

Ser Ser Glu Asn Ser Asn Pro Glu Asn Val Ser Arg Thr Arg Asn Lys
370 375 380

<210> 305
<211> 656
<212> PRT
<213> Homo sapien

<400> 305

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Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
 1               5                  10                  15
Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
            20                  25                  30
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
        35                  40                  45
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
    50                  55                  60
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
65                  70                  75                  80
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
                85                  90                  95
Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
            100                 105                 110
Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
        115                 120                 125
Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
    130                 135                 140
Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
145                 150                 155                 160
Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
                165                 170                 175
Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
            180                 185                 190
Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
        195                 200                 205
Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
    210                 215                 220
Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
225                 230                 235                 240
Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
                245                 250                 255
Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
            260                 265                 270
Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
        275                 280                 285
Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
    290                 295                 300
Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
305                 310                 315                 320
Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
                325                 330                 335
Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
            340                 345                 350
Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
        355                 360                 365
Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu
    370                 375                 380
Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
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385 390 395 400
Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
405 410 415
Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
420 425 430
Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
435 440 445
Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
450 455 460
Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
465 470 475 480
Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
485 490 495
Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
500 505 510
Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys
515 520 525
Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly
530 535 540
Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser
545 550 555 560
Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr
565 570 575
His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln
580 585 590
Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln
595 600 605
Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys
610 615 620
Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile
625 630 635 640
Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
645 650 655

<210> 306
<211> 671
<212> PRT
<213> Homo sapien

<400> 306
Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
1 5 10 15
Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
20 25 30
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
35 40 45
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
50 55 60
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
65 70 75 80
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
85 90 95
Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
100 105 110
Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe

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      115                 120                 125
Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
    130                 135                 140
Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
145                 150                 155                 160
Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
                165                 170                 175
Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
            180                 185                 190
Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
        195                 200                 205
Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
    210                 215                 220
Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
225                 230                 235                 240
Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
                245                 250                 255
Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
            260                 265                 270
Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
        275                 280                 285
Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
    290                 295                 300
Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
305                 310                 315                 320
Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
                325                 330                 335
Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
            340                 345                 350
Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
        355                 360                 365
Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu
    370                 375                 380
Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
385                 390                 395                 400
Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
                405                 410                 415
Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
            420                 425                 430
Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
        435                 440                 445
Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
    450                 455                 460
Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
465                 470                 475                 480
Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
                485                 490                 495
Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
            500                 505                 510
Asn Gly Gln Pro Glu Lys Arg Ser Gln Glu Pro Glu Ile Asn Lys Asp
        515                 520                 525
Gly Asp Arg Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys Lys
    530                 535                 540
His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly Ala
545                 550                 555                 560
```

Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser Arg
565 570 575
Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr His
580 585 590
Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln Asn
595 600 605
Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln Ile
610 615 620
Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys Lys
625 630 635 640
Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile Ala
645 650 655
Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
660 665 670

<210> 307
<211> 800
<212> DNA
<213> Homo sapien

<400> 307
atkagcttcc gcttctgaca acactagaga tccctccact ccctcagggt atggcctcac 60
acttcatttt tggtacataa catctttata ggacaggggt aaaatcccaa tactaacagg 120
agaatgctta ggactctaac aggtttttga gaatgtgttg gtaagggcca ctcaaTgaa 180
tttttcttgg tcctccttgt ggtctaggag gacaggcaag ggtgcagatt ttcaagaatg 240
catcagtaag ggccactaaa tccgaccttc actgttcctc cttgtggtct gggaggaaaa 300
ctagtgtttc tgttgctgtg tcagtgagca caactattcc gatcagcagg gtccagggac 360
cactgcaggt tcttgggcag ggggagaaac aaaacaaacc aaaaccatgg gcrgttttgt 420
ctttcagatg ggaaacactc aggcatcaac aggctcacct ttgaaatgca tcctaagcca 480
atgggacaaa tttgacccac aaaccctgga aaaagaggtg gctcatttttt tttgcactat 540
ggcttggccc caacattctc tctctgatgg ggaaaaatgg ccacctgagg gaagtacaga 600
ttacaatact atcctgcagc ttgacctttt ctgtaagagg gaaggcaaat ggagtgaaat 660
accttatgtc caagctttct tttcattgaa ggagaataca ctatgcaaag cttgaaattt 720
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<210> 308
<211> 102
<212> PRT
<213> Homo sapien

<220>
<221> VARIANT
<222> (1)...(102)
<223> Xaa = Any Amino Acid

<400> 308
Met Gly Xaa Phe Val Phe Gln Met Gly Asn Thr Gln Ala Ser Thr Gly
1 5 10 15
Ser Pro Leu Lys Cys Ile Leu Ser Gln Trp Asp Lys Phe Asp Pro Gln
20 25 30
Thr Leu Glu Lys Glu Val Ala His Phe Phe Cys Thr Met Ala Trp Pro
35 40 45
Gln His Ser Leu Ser Asp Gly Glu Lys Trp Pro Pro Glu Gly Ser Thr
50 55 60

Asp Tyr Asn Thr Ile Leu Gln Leu Asp Leu Phe Cys Lys Arg Glu Gly
65 70 75 80
Lys Trp Ser Glu Ile Pro Tyr Val Gln Ala Phe Phe Ser Leu Lys Glu
85 90 95
Asn Thr Leu Cys Lys Ala
100

<210> 309
<211> 9
<212> PRT
<213> Artificial Sequence
<220>
<223> Made in the lab
<400> 309
Leu Met Ala Glu Glu Tyr Thr Ile Val
1 5

<210> 310
<211> 9
<212> PRT
<213> Artificial Sequence
<220>
<223> Made in the lab
<400> 310
Lys Leu Met Ala Lys Ala Leu Leu Leu
1 5

<210> 311
<211> 9
<212> PRT
<213> Artificial Sequence
<220>
<223> Made in the lab

<400> 311
Gly Leu Thr Pro Leu Leu Leu Gly Ile
1 5

<210> 312
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Made in the lab
<400> 312
Lys Leu Val Leu Asp Arg Arg Cys Gln Leu
1 5 10

<210> 313
<211> 1852
<212> DNA
<213> Homo sapiens

<400> 313
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aaaaccacct atgacaagcc cacagccaac ataatactaa atggggaaaa gttagaagca 120
tttcctctga gaactgcaac aataaataca aggatgctgg attttgtcaa atgccttttc 180
tgtgtctgtt gagatgctta tgtgactttg cttttaattc tgtttatgtg attatcacat 240
ttattgactt gcctgtgtta gaccggaaga gctggggtgt ttctcaggag ccaccgtgtg 300
ctgcggcagc ttcgggataa cttgaggctg catcactggg gaagaaacac aytcctgtcc 360
gtggcgctga tggctgagga cagagcttca gtgtggcttc tctgcgactg gcttcttcgg 420
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(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
19 October 2000 (19.10.2000)

PCT

(10) International Publication Number
WO 00/61753 A3

(51) International Patent Classification[7]: C12N 15/12, C07K 14/47, 16/18, 19/00, C12N 15/62, A61K 38/17, 39/395, 48/00, C12N 5/08, G01N 33/574, C12Q 1/68

(21) International Application Number: PCT/US00/09312

(22) International Filing Date: 7 April 2000 (07.04.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

09/289,198	9 April 1999 (09.04.1999)	US
09/429,755	28 October 1999 (28.10.1999)	US
09/534,825	23 March 2000 (23.03.2000)	US

(71) Applicant: CORIXA CORPORATION [US/US]; Suite 200, 1124 Columbia Street, Seattle, WA 98104 (US).

(72) Inventors: FRUDAKIS, Tony, N.; 7937 Broadmoor Pines Boulevard, Sarasota, FL 34243 (US). SMITH, John, M.; 208 - 116th Place S.E., Everett, WA 98208 (US). REED, Steven, G.; 2843 - 122nd Place N.E., Bellevue, WA 98005 (US). MISHER, Lynda, E.; 6251 53rd Avenue N.E., Seattle, WA 98115 (US). RETTER, Marc, W.; 33402 N.E. 43rd Place, Carnation, WA 98014 (US). DILLON, Davin, C.; 21607 N.E. 24th Street, Redmond, WA 98053 (US).

(74) Agents: POTTER, Jane, E., R.; Seed Intellectual Property Law Group PLLC, Suite 6300, 701 Fifth Avenue, Seattle, WA 98104-7092 et al. (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

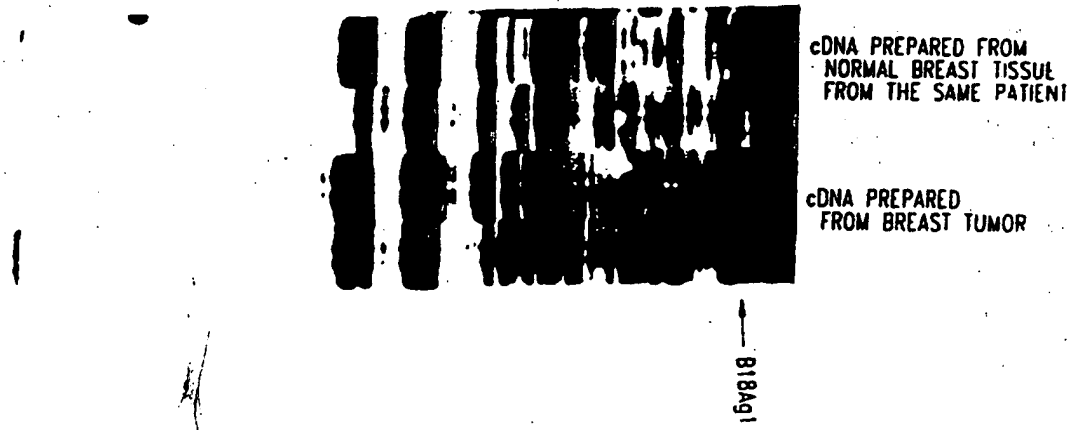
(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *With international search report.*

(88) Date of publication of the international search report:
28 June 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COMPOSITIONS AND METHODS FOR THE TREATMENT AND DIAGNOSIS OF BREAST CANCER



(57) Abstract: Compositions and methods for the detection and therapy of breast cancer are disclosed. The compounds provided include nucleotide sequences that are preferentially expressed in breast tumor tissue, as well as polypeptides encoded by such nucleotide sequences. Vaccines and pharmaceutical compositions comprising such compounds are also provided and may be used, for example, for the prevention and treatment of breast cancer. The polypeptides may also be used for the production of antibodies, which are useful for diagnosing and monitoring the progression of breast cancer in a patient.

WO 00/61753 A3

INTERNATIONAL SEARCH REPORT

Int. .tional Application No
PCT/US 00/09312

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/12 C07K14/47 C07K16/18 C07K19/00 C12N15/62
A61K38/17 A61K39/395 A61K48/00 C12N5/08 G01N33/574
C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K A61K G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 45328 A (CORIXA CORPORATION) 15 October 1998 (1998-10-15) page 2, line 7 -page 5, line 22 page 7, line 23 -page 24, line 11; examples 1-4 sequence listing SEQ ID NOs:1, 3-10, 227 ---	1,2,4-60
X	WO 97 25426 A (CORIXA CORPORATION) 17 July 1997 (1997-07-17) page 2, line 8 -page 5, line 11 page 7, line 14 -page 23, line 2; example 1 sequence listing SEQ ID NO:1, 3-10, 227 --- -/--	1,2,4-60

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 August 2000	08.11.00

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk	

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 25431 A (CORIXA CORPORATION) 17 July 1997 (1997-07-17) page 2, line 3 -page 3, line 25 page 4, line 12 -page 17, line 18; examples 1-4 sequence listing SEQ ID NOs:1, 3-10	1,2,4-10

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/09312

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 21, 22, 29-31 34 37-39 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Claims 1, 2, 4-60 Partially.

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Partially 1, 2, 4-60

Breast cancer related polypeptide B18Ag1, corresponding polynucleotides comprising SEQ ID NOs:1, 3-10, or 227, and derived oligonucleotides; variants thereof, expression vector and host cell comprising the same; antibody and diagnostic kit containing it, fusion protein comprising the polypeptide; pharmaceutical composition and vaccine comprising any of the above and use therefor in the treatment of cancer, and for removing tumor cells from a sample; use of the polypeptides for stimulating and expanding T-cells and use of such T-cells for inhibiting cancer development; use of the polypeptides for determining the presence of cancer or monitoring the progression of cancer in a patient.

2. Claims: Partially 1-60

Idem as subject 1 for Breast cancer related polypeptide and polynucleotide B21GT2 (B311D) comprising SEQ ID NOs:56, 307, 308, 316 or 317.

3. Claims: Partially 1, 2, 4-60

Idem as subject 1 for Breast cancer related polypeptide and polynucleotide B15Ag1 comprising SEQ ID NOs:27 or 290.

4. Claims: Partially 1, 2, 4-60

Idem as subject 1 for Breast cancer related polypeptide and polynucleotide B31GA1b comprising SEQ ID NOs:148.

5. Claims: Partially 1, 2, 4-60

Idem as subject 1 for Breast cancer related polypeptide and polynucleotide B38GA2a comprising SEQ ID NOs:157.

6. Claims: Partially 1-60

Idem as subject 1 for Breast cancer related polypeptide and polynucleotide B11Ag1 (B305D) and its isoform A comprising SEQ ID NO:292-306, or 309-315.

7. Claims: Claims: Partially 1, 2, 4-60, all as far as applicable

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Breast cancer related polypeptides, corresponding polynucleotides comprising SEQ ID NOs:11-26 (inventions 7-22), 28-55 (inventions 23-50), 57-86 (inventions 51-80), 142-147 (inventions 81-86), 149-156 (inventions 87-94), 158-226 (inventions 95-163), 228-253 (inventions 164-189), or 255-291 (inventions 190-226), and derived oligonucleotides; variants thereof, expression vector and host cell comprising the same; antibody and diagnostic kit containing it, fusion protein comprising the polypeptide; pharmaceutical composition and vaccine comprising any of the above and use therefor in the treatment of cancer, and for removing tumor cells from a sample; use of the polypeptides for stimulating and expanding T-cells and use of such T-cells for inhibiting cancer development; use of the polypeptides for inhibiting or monitoring the progression of cancer in a patient, as far as applicable.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9845328 A	15-10-1998	AU 6956098 A	30-10-1998
		EP 0975666 A	02-02-2000
		NO 994932 A	07-12-1999
		PL 336349 A	19-06-2000
		ZA 9802968 A	27-10-1998
WO 9725426 A	17-07-1997	AU 1697497 A	01-08-1997
		BR 9707125 A	20-07-1999
		CA 2242340 A	17-07-1997
		CN 1211279 A	17-03-1999
		EP 0874902 A	04-11-1998
		NO 983183 A	10-09-1998
WO 9725431 A	17-07-1997	AU 1575697 A	01-08-1997